DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Center for Tobacco Products
10903 New Hampshire Avenue
Silver Spring, MD 20993

December 11, 2017

PRELIMINARY FINDING

[redacted]
Attention: [redacted]
[redacted]

FDA Submission Tracking Number (STN): [redacted]

Dear [redacted]:

We have completed our review of your Substantial Equivalence (SE) Report, with the exception of the environmental assessment. This review includes an evaluation of timely amendments to that report. We have preliminarily determined that the SE Report does not in its present form support a determination of substantial equivalence. Below, we have described the deficiencies that led to this determination and, where possible, our recommendations to address these issues.

Please refer to your December 19, 2016, Report Preceding Introduction of Certain Substantially Equivalent Products into Interstate Commerce (SE Report), submitted under section 905(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for [redacted].

We also refer to your following amendments:

- March 16, 2017, containing your responses to FDA's Preliminary Finding letter dated March 14, 2017
- March 29, 2017, containing corrections to product information
- August 17, 2017, containing your "stay request" to respond to FDA's Advice/Information Request (A/I) letter dated June 27, 2017
- August 26, 2017, containing your responses to FDA's A/I Request letter dated June 27, 2017

Based on our review of your SE Report, the following information is not included and is needed in order for FDA to make a determination as to whether your SE Report establishes substantial equivalence:

1. Your SE Report provides information on the design parameters for the new and predicate products. However, it does not include all of the design parameters necessary to fully characterize the new and predicate products. You state that you do not have the design parameter target specifications and upper and lower range limits for the new and predicate product. However, in order to adequately characterize the products, it is

necessary to compare key design parameters. Provide the target specification and upper and lower range limits for all of the following design parameters for the new and predicate product:

a. Cigar draw resistance (mm H_2O)
b. Tobacco filler mass (mg)
c. Tobacco rod density (g/cm^2)
d. Tobacco moisture (%)
e. Wrapper mass (mg)
f. Binder mass (mg)

Additionally, provide the upper and lower range limits for all of the following design parameters for the new and predicate product:

g. Cigar length (mm)
h. Cigar maximum diameter (mm)

For each of the above parameters, provide the necessary data on a per unit of measurement of product basis (e.g., wrapper mass should be in mg per cigar). If a design parameter is not applicable (e.g., binder mass, if the cigar does not contain binder), state as such and provide an explanation for why the design parameter is not applicable.

If a difference exists in the target specifications or range limits between the new and predicate product, provide scientific evidence and a rationale for why the difference(s) does not cause the new product to raise different questions of public health.

2. Your SE Report includes design parameter specifications, but does not include data confirming that specifications are met. You state that you do not have the design parameter test data for the new and predicate products. However, test data is necessary in order to confirm that design parameter specifications have been met. Therefore, provide the test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for all of the following design parameters for the new and predicate product:

a. Puff count
b. Cigar draw resistance (mm H_2O)
c. Tobacco filler mass (mg)
d. Tobacco moisture (%)

For each of the above parameters, provide the necessary data on a per unit of measurement of product basis (e.g., puff count should be reported in puff count per cigar). If a design parameter is not applicable, state as such.

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

3. Your SE Report does not include all of the design parameters necessary to fully characterize the new and predicate products and data to confirm that specifications are met. You state that you do not have the design parameter specifications and test data for the new and predicate products. However, design parameter target specifications, upper and lower range limits, and test data are necessary in order to adequately characterize the products and confirm that design parameter specifications have been met. Therefore, provide the target specifications, upper and lower range limits, and test data (i.e., measured values of design parameters), including test protocols, quantitative acceptance criteria, data sets, and a summary of the results for all of the following design parameters for the new and predicate product:

    a. Wrapper basis weight (g/m^2)
    b. Wrapper porosity (CU)
    c. Binder basis weight (g/m^2)
    d. Binder porosity (CU)

    For each of the above parameters, provide the necessary data on a per unit of measurement of product basis (e.g., puff count should be reported in puff count per cigar). If a design parameter is not applicable (e.g., binder porosity), state as such and provide an explanation for why the design parameter is not applicable.

    If you cannot provide target specifications, upper and lower range limits, or test data for the wrapper basis weight, wrapper porosity, binder basis weight, or binder porosity for the new and predicate products, provide information to demonstrate that there are no differences in the wrapper and the binder between the new and predicate products that would cause the new product to raise different questions of public health. Although there may be other ways to satisfy this deficiency, one way would be to provide a detailed side-by-side comparison of the tobacco wrapper and binder origin (e.g. tobacco plant variety and leaf characteristics), dimensions, and processing parameters for the new and predicate products. The comparison should include a justification for why any minor differences in the characteristics and processing of the wrapper and binder do not cause the new product to raise different questions of public health.

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

4. Your SE Report includes the same tobacco type (i.e., dark tobacco) but different tobacco varieties (e.g., [redacted]

[redacted]without including tobacco quantities for each tobacco variety. Additionally, you stated that "no specific grading system is used" except for using "smell and physical characteristics of the leaf" in the leaf selection without explaining what the "smell and physical characteristics" are (e.g., whether tobacco color, stalk position, or any other factors are included as the physical characteristics); whether they are the same or different for the new and predicate products; and whether they are known to the product manufacturers to have impact on the tobacco blend nicotine strengths, burning characteristics, and wrapper colors. The general cigar manufacturer and user observation reveals that 1) each dark tobacco variety may be unique in its nicotine content; and 2) cigar tobacco priming, as part of the grade information, may affect the tobacco burning characteristics and nicotine strength. Without the quantity of each tobacco variety, the tobacco variety characteristics known to the product manufacturers, and the full information regarding the "smell and physical characteristics" used in leaf selection for the new and predicate products, FDA is not able to compare the new and predicate products. For FDA to fully understand and compare the new and predicate products, provide a side-by-side comparison of the following for the new and predicate products:

a. The quantity for tobacco subcomponents (i.e., filler, binder, and wrapper) and each tobacco variety (also known as "cigar tobacco types" per cigar users) used for the new and predicate products
b. The qualitative tobacco variety characteristics known to the new and predicate product manufacturers in nicotine strength (e.g., [redacted])
c. Full information for the "smell and physical characteristics" the blend masters use in the leaf selection for the new and predicate products (e.g., what smell is used and what the physical characteristics are)
d. The impact, known to the cigar manufacturers, of the "smell and physical characteristics" on the burning characteristics and the nicotine strength of the new and predicate products, if applicable. If no such impact exists, state as such
e. Tobacco stalk positions used and wrapper colors

If the listed information for the new and predicate products differs, provide evidence and a scientific rationale for why the difference(s) does not cause the new product to raise different questions of public health.

5. Your SE Report includes the identity and estimated quantity for the glue (i.e., Sodium carboxymethyl cellulose (CMC)). However, your response lacks the purity information for CMC and is not clear whether the estimated glue quantity is intended for the new, predicate or both products. Based on your description, CMC is applied to the closed tip of your new product, which implies that CMC may be in contact with the users' mouth. Therefore, quality (e.g., percent purity or grade) information is needed to evaluate its safety. Additionally, you provided a justification for why the glue is not burnt during product use based on your occasional and individual cigar use experience, which is not specific to the new and predicate products and lacks objective scientific evidence. It is not clear why your experience reflects user behavior of a representative user population

of the new and predicate products. For FDA to fully understand the new and predicate products and evaluate whether the new and predicate products are substantially equivalent based on evidence and scientific rationales, provide a side-by-side comparison of the following for the new and predicate products:

a. Purity or grade of the CMC used
b. A clarification as to whether the quantity of CMC (0.01 ounces/cigar) is submitted for the new, predicate, or both products
c. The numeric location (i.e., distance from where CMC is applied to the covered end of the new and predicate products) of CMC
d. The butt length (i.e., the length of unburnt cigar remaining when the smoking is stopped)

If the information listed above is identical for the new and predicate products, state as such and provide the listed information for the new product. If the listed information for the new and predicate products differs, provide evidence and a scientific rationale for why the difference(s) does not cause the new product to raise different questions of public health.

6. Your SE Report states that the new and predicate tobacco products use the same methods of fermentation, stopping fermentation and storage. However, your SE Report lacks specific information regarding the fermentation process, the conditions of fermentation, methods used to stop the fermentation process and storage conditions of the final new and predicate tobacco products. Information about the fermentation process is needed because fermentation can result in different degrees of change in the chemical constituents of the tobacco as well as impact the microbial content of the final product. Provide the fermentation specifications including, but not limited to:

a. Location of fermentation (open-air vs closed system)
b. Batch size and duration of fermentation
c. Fermentation conditions (e.g., pH, temperature, humidity, airflow)
d. Microbial characterization data (including species name and inoculum concentration) of the fermentation inoculum/starter cultures, if applicable
e. Indicate if any of the physical or microbial factors are controlled during fermentation
f. Ingredients added during the fermentation process that would impact the microbial stability of the product, if applicable
g. Method used to stabilize or stop fermentation (e.g., heat treatment, cooling) including the parameters of the method (e.g., length of treatment, temperature)
h. Storage conditions of the final products prior to and post packaging

Provide this information for the new and predicate tobacco products. If this information is identical for the new and predicate tobacco products, provide information for the new tobacco product and a statement that the information is identical for the predicate tobacco product. If there are differences, explain why those differences do not cause the new tobacco product to raise different questions of public health.

7. Your SE Report states that the new and predicate tobacco products are manufactured using a fermentation process; however, your SE Report lacks post-manufacturing stability information for the new and predicate tobacco products. Tobacco specific nitrosamines (TSNAs) are primarily formed during tobacco curing and fermentation of the processed tobacco, as well as during aging/storage of the processed and packaged tobacco product. Factors such as nitrate and nitrite concentrations, moisture content, microbial content, pH, and storage temperature are reported to influence microbial stability and TSNA formation during storage of tobacco products. Provide a detailed description of all stability testing performed, including test protocols, quantitative acceptance criteria, data sets and a summary of the results. Provide microbial content data to include total aerobic microbial count (TAMC) and total yeast and mold count (TYMC) for the expected storage period of the new and predicate tobacco products. In addition to microbial content, provide stability testing data for the physical and chemical attributes which affect microbial activity during product storage. At a minimum, provide measurements for all of the following:

    a. pH
    b. Water activity (a_w)
    c. Moisture content
    d. TSNAs (total, NNN, NNK)
    e. Nitrate and nitrite
    f. Preservatives and microbial metabolic inhibitor levels, if any
    g. TAMC
    h. TYMC

    Measurement of these parameters should be made at the beginning (zero time), middle, and end of the expected storage time for the final new and predicate tobacco products. This information is required to determine whether the new and predicate tobacco products are substantially equivalent. The accuracy, sensitivity, specificity and reproducibility of the test methods should be determined and documented. Explain how the expected storage time is determined. If there are differences in any of these endpoints for the new and predicate tobacco products, explain why those differences do not cause the new tobacco product to raise different questions of public health.

Please be advised that an inadequate resolution of the issues in your next response, or lack of timely response, will likely result in a not substantially equivalent determination. We will evaluate the information included in your timely response to this letter prior to finalizing our review of your SE Report. Alternatively, you may submit a request to withdraw this SE Report. If you do not take one of these actions, we will finalize our decision on your SE Report based on the information you have previously submitted.

If you receive a finding of not substantially equivalent or choose to withdraw the SE Report for this new tobacco product, you may seek an FDA order to market the product by submitting a new SE Report, a request for exemption from substantial equivalence (if applicable under 21 CFR 1107.1), or an application for premarket review of new tobacco products

(section 910(b)(1) of the FD&C Act). See the following website for additional information on these three pathways: http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/default.htm.

In addition to the above required information, we request the following additional information to assist in our scientific review:

8. Your SE Report includes the same tobacco type (i.e., dark tobacco) but different tobacco varieties (e.g., [redacted]). The general cigar manufacturer and user observation reveals that each dark tobacco variety may be unique in its nicotine content. It is unclear whether this uniqueness of the tobacco variety and the use of different tobacco variety for the new and predicate product generate difference in nicotine content in the new and predicate products. Measuring the nicotine content in the tobacco used to manufacture the new and predicate products may provide helpful information for FDA to understand better the new and predicate products. In doing so, FDA suggests that appropriate measures be taken to minimize data variability and systematic bias. The suggested measures include, but not limited to, using the same laboratory, the same methods, similar sample storage conditions and duration, and testing within similar timeframe. Provide the following information about nicotine testing so that FDA can fully evaluate the differences in nicotine quantities between the new and predicate products:

    a. Reference product datasets
    b. Quantitative test protocols and method used
    c. Testing laboratory and their accreditation(s)
    d. Method validation status and complete validation reports
    e. Deviations from national or international standards, if they are used
    f. Length of time between date(s) of manufacture and date(s) of testing
    g. Number of replicates
    h. Standard deviation(s)
    i. Complete data sets
    j. A summary of the results for all testing performed
    k. Storage conditions prior to initiating testing

Your environmental assessment is currently under review. If there are additional items contained in your environmental assessment that require clarification or information, we will notify you.

Section 910(a)(4) of the FD&C Act requires each submission under section 905(j) of the FD&C Act to "provide an adequate summary of any health information related to the tobacco product or state that such information will be made available upon request by any person. Any summary . . . shall contain detailed information regarding data concerning adverse health effects…" Accordingly, section 910(a)(4) of the FD&C Act will enable the public to obtain adverse health effects information related to your product.

To be an "adequate summary," any provided summary should be accurate and complete, and not false or misleading, to members of the public who might review it. Please note, as well, that the requirement to provide data concerning adverse health effects is not limited to specific adverse events that have been reported to you, but rather includes any research or data concerning adverse health effects of which you are aware.

Consistent with the requirements of section 910(a)(4) of the FD&C Act, you may take one of the following approaches in your SE Report:

A. Provide an accurate, complete, not false or misleading summary to FDA that includes *all* of the following:

    i. Description of the new tobacco product;
    ii. Description of the predicate tobacco product;
    iii. List of all differences in characteristics between the predicate and new tobacco products;
    iv. Summary of the evidence and scientific rationale concerning why the differences in characteristics do not raise different questions of public health; and
    v. Any research or data you have in your possession or otherwise know of regarding the adverse health effects of the new tobacco product *or* the following statement if such statement is accurate: "[Insert manufacturer name] does not have or know of any research or data regarding any adverse health effects specifically related to [insert tobacco product name]."

B. Truthfully state that you will provide the information described in section 910(a)(4) of the FD&C Act, upon request, to any person, and in response to all such requests provide the information listed in item A.i.-v., above.

C. Truthfully state that you will provide the information described in section 910(a)(4) of the FD&C Act, upon request, to any person, and in response to all such requests provide the following information to requestors:

    i. A copy of your SE Report, redacted only to the extent necessary to exclude research subject identifiers, and trade secret and confidential commercial information as defined in 21 CFR 20.61 and 20.63 and
    ii. The information in item A.v., above.

There may be other accurate, complete and not false or misleading ways to satisfy the requirements of section 910(a)(4) of the FD&C Act, and FDA will consider other approaches on a case-by-case basis.

As stated above, any statement you are required to include within a health information summary pursuant to section 910(a)(4) of the FD&C Act would not constitute a modified risk claim under section 911 of the Act. However if your health information summary contains a statement that is outside the requirements of 910(a)(4) that "would be reasonably expected to result in consumers believing that the tobacco product or its smoke may present a lower risk of disease or is less

harmful than one or more commercially marketed tobacco products, or presents a reduced exposure to, or does not contain or is free of, a substance or substances," such a statement may constitute a modified risk claim under section 911 of the FD&C Act.

If your health information summary or the health information you provide to requestors, rather than submitting a summary to FDA, includes information outside the requirements of 910(a)(4) that causes your product to be in violation of section 911 of the FD&C Act, your product would be adulterated under section 902 of the FD&C Act. Similarly, if your health information summary includes information that is false or misleading, the product may be misbranded under section 903 of the FD&C Act. Violations of the FD&C Act are subject to regulatory and enforcement action by FDA including, but not limited to, seizure and injunction.

We request that you submit all the information identified above so that it is <u>received</u> by us no later than 30 days from the date of this letter. Your information should be sent as a single submission with a cover letter that includes the following text in your subject line: **RESPONSE TO PRELIMINARY FINDING for** [redacted]. When responding, we request your submission be organized in the following manner so that we can easily identify your responses to each numerated item above:

- List each number and full deficiency text as stated above, and provide your response immediately following the deficiency
    - If submitting a large amount of data to address a deficiency, submit the data as an appendix/appendices and reference the appropriate appendix/appendices in your response
    - If submitting publication(s) to address a deficiency, submit the publication(s) as an appendix/appendices and reference the appropriate appendix/appendices in your response
    - If resubmitting information previously submitted (e.g., tables) to correct earlier omissions/errors, clearly identify what information has been revised
    - If you have already submitted any of the information requested in the deficiency, identify the date of the prior submission, page number(s), and line numbers where the requested information is located
- All pages in your submission should be consecutively numbered

We encourage you to submit all regulatory correspondence electronically via the CTP Portal (http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Manufacturing/ucm515047.htm)[1] using eSubmitter (http://www.fda.gov/ForIndustry/FDAeSubmitter). Alternatively, submissions may be mailed to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center (DCC)
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

[1] The FDA's Electronic Submission Gateway (ESG) is still available as an alternative to the CTP Portal.

The CTP Portal and FDA Electronic Submission Gateway (ESG) are both generally available 24 hours a day, seven days a week. Submissions delivered to DCC by couriers or physical mail will be considered timely if received during delivery hours on or before the due date (see http://www.fda.gov/tobaccoproducts/aboutctp/contactus/default.htm); if the due date falls on a weekend or holiday the delivery must be received on the prior business day. We are unable to accept regulatory submissions by e-mail.

As long as your product was on the U.S. market as of the effective date of the deeming rule (August 8, 2016), FDA does not intend to object to the commercial distribution of the new product described in this SE Report as long as you have submitted an application under 905(j)(3) or 910(a)(2) by August 8, 2021 and FDA has not issued an order denying or refusing to accept the submission, after August 8, 2021.[2] FDA will otherwise notify you if this changes.

If you have any questions, please contact Elizabeth Bryan, Regulatory Health Project Manager, at (240) 402 - 5639.

Sincerely,

Todd L. Cecil -S Digitally signed by Todd L. Cecil -S
Date: 2017.12.11 10:31:04 -05'00'

Todd L. Cecil, Ph.D.
Associate Director, Division of Product Science
Office of Science
Center for Tobacco Products

[2] Refer to FDA's November 2017 Revised Guidance for Industry entitled "Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule" which extends the time period by three months.