U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

May 12, 2020

NOT SUBSTANTIALLY EQUIVALENT

R.J. Reynolds Tobacco Company
Attention: Michael W. Ogden, Ph.D.
Senior Vice President, Scientific & Regulatory Affairs
RAI Services Company
401 North Main Street
Winston-Salem, NC 27101

FDA Submission Tracking Number (STN): SE0000279, see Appendix A

Dear Dr. Ogden:

We completed our review of your SE Report[1] and determined that the new tobacco product is not substantially equivalent to the predicate tobacco products listed in Appendix A. Refer to Appendix B for a list of amendments received in support of your application.

Your SE Report includes information for an additional predicate tobacco product (Camel Snus Frost) that you identified in your April 3, 2015, amendment as a predicate tobacco product. Information for this additional predicate tobacco product is provided alongside information for the new and predicate tobacco products identified in the SE Report at the time scientific review commenced. Because the comparison between the new tobacco product and the identified predicate tobacco product is a fundamental aspect of an SE Report, changing the predicate tobacco product changes the basis of the substantial equivalence evaluation. An applicant may change its predicate tobacco product if scientific review of the application has not yet started. However, once FDA commences scientific review, an applicant should not change its predicate tobacco product(s); the application review will be based on the comparison between the predicate tobacco product(s) in place at the start of scientific review and the new tobacco product. Therefore, the additional predicate tobacco product, Camel Snus Frost, that you identified was not considered in FDA's evaluation of your SE Reports. FDA issued a Notification Letter on March 29, 2013, which notified you that scientific review was scheduled to begin on May 15, 2013; therefore, you had the opportunity to change your predicate tobacco product up to May 14, 2013. You provided an amendment on May 14, 2013, which identified Dental Scotch (dry snuff) and Grizzly Long Cut Mint (moist snuff) as your predicate tobacco products. The deficiencies listed in this letter reflect a comparison of the characteristics of the new tobacco product to the characteristics of each individual predicate tobacco product that you identified at the start of FDA's scientific review, Dental Scotch and Grizzly Long Cut Mint.

[1] Substantially Equivalent (SE) Report submitted under section 905(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

The following deficiencies are the basis for our determination:

1. The length of time between the manufacture of the new tobacco product and the conduct of harmful and potentially harmful constituent (HPHC) testing (18-24 months after manufacture) is approximately 6 to 12 months longer than that for predicate tobacco product 1 (Dental Scotch) and approximately 10 to 12 months longer than that for predicate tobacco product 2 (Grizzly Long Cut Mint). Your SE Report lacked an explanation on how the length of time before testing would impact the comparison of HPHC data between the new and predicate tobacco products. You stated that the length of time between manufacture and testing of the new tobacco product was longer than the "reasonably expected shelf-life" and could be "considered as a "worst case scenario"." Your statement appears to be based on an assumption that, at the time of the HPHC testing, the HPHC levels were the highest/worst for the new tobacco product and the lowest/best for the predicate tobacco products. You did not provide evidence demonstrating the validity of this assumption. For certain smokeless tobacco products, HPHC levels, such as nicotine, may decrease over time. To be able to evaluate and determine the differences in HPHC levels, FDA needed either HPHC data from the new tobacco product and the predicate tobacco products that had comparable lengths of time between their manufacture and their testing, or scientific evidence explaining how different lengths of time between the tobacco products' manufacture and testing would impact the comparison of HPHC data. Without this information, the SE Report lacks adequate evidence to demonstrate that the changes in product design and composition do not cause the new tobacco product to raise different questions of public health.

2. Your SE Report lacks stability or shelf-life study information for the predicate tobacco products. A detailed description of stability testing, including test protocols, quantitative acceptance criteria, data sets and a summary of the results for all stability testing performed over the complete storage time of the new and each predicate tobacco product was necessary to assess the new and predicate tobacco products. At a minimum, FDA needed measurements for all of the following for each predicate tobacco product:

    a. pH;
    b. Water activity (a_w);
    c. Moisture content;
    d. TSNAs (total, NNN, NNK);
    e. Nicotine content; and
    f. Bacterial load

    Ideally, measurements of these parameters should have been made at the beginning, middle, and end of the expected storage time and at the expected storage conditions of the tobacco products. If any of the measurements of stability had differed between the new and predicate tobacco products, evidence and scientific rationale demonstrating that these differences do not cause the new tobacco product to raise different questions of public health were needed.

3. Your SE Report includes a summary of comparisons from the National Tobacco Behavior Monitor (NTBM) survey from May 2010 to December 2014 which is provided to justify that changes in flavor ingredients and product format do not influence tobacco use behavior between users of the new tobacco product compared to predicate tobacco product 2 (Grizzly Long Cut Mint). However, your SE Report did not include enough information about the NTBM methodology and data analyses to evaluate whether the summarized comparisons can be bridged to your new tobacco product. FDA needed complete information and rationale for the

NTBM and the submitted Oliver paper[2] sample sizes, sample demographic and tobacco use behavior, and data analyses and how they pertain to the new tobacco product, such as initiation among non-users, or increased use or decreased cessation among users when comparing the predicate tobacco products to the new tobacco product. Further, a scientific rationale and evidence were needed to demonstrate whether the product format, flavor ingredients, and package quantity changes between predicate tobacco product 2, (Grizzly Long Cut Mint), and the new tobacco product affected product consumption frequency and rate, tobacco initiation and recidivism prevalence, or intention to quit all tobacco by users. Additionally, no comparisons were included to predicate tobacco product 1, (Dental Scotch). Your SE Report was not sufficient to address how the stated change in flavor ingredients and product format would not cause the new tobacco product to raise different questions of public health. Without this information, the SE Report lacks evidence to demonstrate that the differences in flavor ingredients and product format do not cause the new tobacco product to raise different questions of public health as compared to the predicate tobacco products related to tobacco use behavior.

4. Your SE Report includes information from clinical trials and survey data to address changes in free nicotine, nicotine release rates, menthol, binders, and coatings in the new tobacco product compared to the predicate tobacco products. However, the "Fresh" predecessor tobacco products used in the clinical studies may be different than the "mint" new tobacco product. Your Product Stewardship Reports note that there are "differences in the ingredients added to [the] tobacco," or that there is a "modified recipe" as compared to the "Fresh"-flavored product. In addition, you suggested that the new tobacco product shared similarities with the Fresh predecessor tobacco products but provided no information or evidence to support this assertion. Therefore, the submitted data cannot be bridged to the new tobacco product. Without the additional data and information, the SE Report lacks adequate evidence to demonstrate that the changes to the product constituents do not cause the new tobacco product to raise different questions of public health.

Your SE Report lacks sufficient information to support a finding of substantial equivalence; therefore, we are issuing an order finding that this new tobacco product is not substantially equivalent to an appropriate predicate tobacco product. Upon issuance of this order, your tobacco product is misbranded under section 903(a)(6) of the FD&C Act and adulterated under section 902(6)(A) of the FD&C Act. Failure to comply with the FD&C Act may result in FDA taking regulatory action without further notice. These actions may include, but are not limited to, civil money penalties, seizure, and/or injunction.

To provide time for a sell-off of the product that is the subject of this NSE order, FDA does not intend to take an enforcement action for at least 30 calendar days from the date of this letter. FDA does not intend to post notice of this NSE order on its misbranded and adulterated NSE Tobacco Products website unless and until it affirms the NSE order. This compliance policy does not extend to FD&C Act requirements other than the requirement of premarket review. For more information, see https://www.fda.gov/tobacco-products/compliance-enforcement-training/manufacturing.

FDA requests that, **within 15 days** of this letter, you submit a plan detailing the steps that you plan to take to ensure that these misbranded and adulterated product is not further distributed, imported, sold, marketed, or promoted in the United States by others. Your plan should include information sufficient to distinguish these misbranded and adulterated product from legally marketed tobacco

[2] Oliver, A.J., Jensen, J.A., Vogel, R.I., Anderson, A.J., Hatsukami, O.K. (2013) Flavored and nonflavored smokeless tobacco products: rate, pattern of use, and effects. *Nicotine Tob. Res.* Jan: 15(1): 88-92.

products, including, but not limited to lot numbers, manufacturing codes, and manufacturing dates. The plan should also include a list of your direct accounts and associated contact information. Submit your plan to the address below with a cover letter that includes the following text in the subject line:

COMPLIANCE PLAN for SE0000279

FDA will post product information on its misbranded and adulterated NSE Tobacco Products website, available to the public. For more information, see https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/misbranded-and-adulterated-nse-tobacco-products.

We remind you that you are required to update your listing information in June and December of each year under section 905(i)(3) of the FD&C Act. As part of this listing update, under section 905(i)(3)(B) of the FD&C Act, you must provide information on the date of discontinuance and product identity for any product you discontinue.

We encourage you to submit all regulatory correspondence electronically via the CTP Portal[3,4] using eSubmitter.[5] 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

The CTP Portal and FDA's Electronic Submission Gateway (ESG) are generally available 24 hours a day, seven days a week; submissions are considered received by DCC on the day of successful upload. Submissions delivered to DCC by courier or physical mail will be considered timely if received during delivery hours on or before the due date[6]; if the due date falls on a weekend or holiday, the delivery must be received on or before the preceding business day. We are unable to accept regulatory submissions by e-mail.

If you have any questions, please contact Barbara Banchero, Regulatory Health Project Manager, at (301) 796-1937 or Barbara.Banchero@fda.hhs.gov.

Sincerely,

Digitally signed by Matthew R. Holman -S
Date: 2020.05.12 17:14:43 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science
Center for Tobacco Products

[3] For more information about CTP Portal, see https://www.fda.gov/tobacco-products/manufacturing/submit-documents-ctp-portal
[4] FDA's Electronic Submission Gateway (ESG) is still available as an alternative to the CTP Portal.
[5] For more information about eSubmitter, see https://www.fda.gov/industry/fda-esubmitter
[6] https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/contact-ctp

Enclosures:

Appendix A – New and Predicate Tobacco Products Subject of This Letter
Appendix B – Amendments Received for This Application

Appendix A

New and Predicate Tobacco Products Subject of This Letter

Attributes of SE Report			
Date of Submission:	March 18, 2011		
Date of Receipt:	March 18, 2011		
Product Manufacturer:	R.J. Reynolds Tobacco Company		
Product Category:	Smokeless Tobacco Products		
	New Tobacco Product	**Predicate Tobacco Product**	**Predicate Tobacco Product**
	SE0000279: Camel Strips Mint[7,8]	**GF1200379: Dental Scotch[7]**	**GF1200410: Grizzly Long Cut Mint[7]**
Product Manufacturer	R.J. Reynolds Tobacco Company	American Snuff Company, LLC	American Snuff Company, LLC
Product Sub-Category:	Dissolvable	Loose Dry Snuff	Loose Moist Snuff
Package Type:	Plastic Can and Plastic Lid	Can (fiberboard and metal)	Plastic Can and Plastic Lid
Package Quantity:	2.88 g	1.15 oz	1.2 oz
Characterizing Flavor:	Mint	None	Mint
Eligibility Status:	N/A	Grandfathered	Grandfathered
Portion Count:	12 Strips	Not Applicable	Not Applicable
Portion Mass:	240 mg	Not Applicable	Not Applicable
Portion Length:	32 mm	Not Applicable	Not Applicable
Portion Width:	22 mm	Not Applicable	Not Applicable
Portion Thickness:	0.5 mm	Not Applicable	Not Applicable
Tobacco Cut Size:	(b) (4) µm	(b) (4) µm	(b) (4) µm

[7] Brand/sub-brand or other commercial name used in commercial distribution.

[8] Providing portion mass plus two of the three portion dimensions (along with other specified properties) will allow for full identification of portioned moist snuff, snus, chewing, and dissolvable products.

Appendix B

Amendments Received for This Application

Amendments Received	
Date of Submission:	November 15, 2012
Date of Receipt:	November 16, 2012
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Response to October 25, 2012, FDA Information Request
Date of Submission:	May 14, 2013
Date of Receipt:	May 14, 2013
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Response to March 29, 2013, FDA Information Request
Date of Submission:	March 21, 2014
Date of Receipt:	March 26, 2014
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Request for extension to respond to March 18, 2014, FDA Information Request
Date of Submission:	April 2, 2014
Date of Receipt:	April 2, 2014
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Response to March 26, 2014, FDA Information Request
Date of Submission:	May 16, 2014
Date of Receipt:	May 16, 2014
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Response to March 18, 2014, Deficiency Letter

Date of Submission:	March 6, 2015
Date of Receipt:	March 9, 2015
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Request for extension to March 4, 2015, Deficiency Letter
Date of Submission:	April 3, 2015
Date of Receipt:	April 3, 2015
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Response to March 4, 2015 Deficiency Letter
Date of Submission:	May 14, 2015
Date of Receipt:	May 15, 2015
Reviewed:	Yes
SE Report being amended:	SE0000279
Status:	Active
Brief Description:	Correction to April 3, 2015 amendment