



RAI Services Company

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Hans Rosenfeldt, Ph.D.
Deputy Director, Division of Nonclinical Science
Deirdre Kittner, Ph.D., MPH
Deputy Director, Division of Population Health Science
Office of Science
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

**Re: PARTIAL RESPONSE (DEFICIENCY 8) to AUGUST 10, 2018 ADVICE/INFORMATION REQUEST
for PM0000427-PM0000432 and MR0000068-MR0000073**

Dear Drs. Rosenfeldt and Kittner:

RAI Services Company ("RAIS")¹ hereby submits the following, on behalf of R.J. Reynolds Tobacco Company ("RJRT"), in response to the United States Food and Drug Administration's ("FDA") Center for Tobacco Products ("CTP") August 10, 2018, ADVICE/INFORMATION REQUEST letter regarding RAIS's submission of Premarket Tobacco Applications ("PMTAs") and Applications Seeking a Modified Risk Tobacco Product Order ("MRTP Applications"), submitted under Section 910(b) and Section 911(d) of the Food, Drug, and Cosmetic Act ("FDCA"), respectively, on March 30, 2017 for the following tobacco products:

- PM0000427/MR0000072, Camel Snus Robust
- PM0000428/MR0000070, Camel Snus Mellow

¹ RAI Services Company ("RAIS") bears primary responsibility for regulatory compliance for Reynolds American Inc.'s operating companies, including R.J. Reynolds Tobacco Company ("RJRT"), American Snuff Co., LLC ("ASC"), Santa Fe Natural Tobacco Company, Inc. ("SFNTC"), and R.J. Reynolds Vapor Company ("RJRV"). References to RAIS in this letter refer to itself and RJRT where applicable.

- PM0000429/MR0000069, Camel Snus Frost Large
- PM0000430/MR0000071, Camel Snus Mint
- PM0000431/MR0000073, Camel Snus Winterchill
- PM0000432/MR0000068, Camel Snus Frost

This response refers to Deficiency Eight (8) in the aforementioned ADVICE/INFORMATION REQUEST. Deficiencies not addressed in this submission will be covered in separate responses. In this response, we have repeated CTP's requests, verbatim and in bold italics, followed by RAIS's response.

Please note that the enclosed response may contain confidential commercial and non-public trade secret information belonging to RAIS, RJRT, or RJRT's vendors. All such confidential and trade secret information is exempt from public disclosure under § 301(j) and § 906(c) of the FDCA, 5 U.S.C. § 552(b)(4), 18 U.S.C. § 1905, and 21 C.F.R. § 20.61 and any similar or related laws and regulations. RAIS and RJRT respectfully request that FDA maintain the confidentiality of this information.

Should you have any questions or require any additional information, please contact me at your earliest convenience.

Respectfully submitted,



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8. *All of your MRTPAs/PMTAs provide some microbial activity data (aw, TAMC, TYMC, and total coliform bacteria); however, you provide long-term stability (i.e., aging) data, which includes moisture, pH, NNN, NAT, NAB, NNK, and total TSNA's, for only one product, Camel Snus Winterchill (MR0000073/PM0000431). Explain how the long-term stability data from Camel Snus Winterchill can be extrapolated to the other five tobacco products given that Camel Snus Winterchill has the lowest mean water activity compared to the other tobacco products and contains different ingredients,* (b) (4)

(b) (4) *Another way to help address long-term stability would be to provide measurements of the following for each product:*

- a. *pH;*
- b. *moisture; and*
- c. *TSNA's (total, NNN, NNK).*

At a minimum, measurement of these parameters should be made at the beginning, middle, and end of the expected storage time. Provide full test data (including test protocols, quantitative acceptance criteria, data sets, and a summary of the results) for all testing performed. The accuracy, sensitivity, specificity and reproducibility of the test methods should be determined, and documented, as well as reported to FDA.

RAIS GENERAL RESPONSE TO DEFICIENCY 8

RAIS understands FDA's request to be for stability test data for each product subject of these applications. Specifically, FDA requests information regarding pH, moisture content, and TSNA's (total, NNN, NNK), over the expected storage time of each product.

FDA indicates that RAIS may satisfy this deficiency by providing stability measurements for each product, and since the submission of the MRTPAs/PMTAs, RAIS has concluded a stability study for all products that are subject of this submission. These studies were previously submitted to FDA in the July 23, 2018 amendment and include the data requested in this deficiency. However, RAIS has determined that there was a typographical error in the graphs for all Camel Snus styles for arsenic which contained cadmium data. As such, RAIS is submitting a revision of the internal study report ([d08-rdm-trm-2018-192-b](#), [RDM TRM 2018 192-b](#))². All other data within that report is identical to what was submitted in the July 23, 2018 amendment. Given that RAIS is providing product specific information for each of the Camel Snus variants, as suggested by FDA, we will only discuss the stability study herein and will not address FDA's deficiencies related to extrapolation of them from the long-term stability study for Camel Snus Winterchill.

(b) (4)

² RAIS notes that [RDM TRM 2018 192-b](#) is the most current version of the report. Upon review, RAIS has identified typographical errors in this report. These errors and their corrections are provided in [d08-air-mr68-73-pm427-432-rdm-corrections](#)

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(b) (4)



(b) (4)



(b) (4)



¹ ICH; *Guidance for the Industry Q1A(R2) Stability Testing of New Drug Substances and Products*; November 2003:
<https://www.fda.gov/downloads/drugs/guidances/ucm073369.pdf>

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PM0000427- PM0000432/MR0000068-MR0000073 A/I PARTIAL RESPONSE – DEFICIENCY 8

(b) (4)



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Stability Study Design

(b) (4)



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(b) (4)

Table 2: Camel Snus Statistical Summaries	
Camel Snus Variety	Location within Stability Report (d08-rdm-trm-2018-192-b)
Camel Snus Robust	Appendix K, Page 700
Camel Snus Mellow	Appendix I, Page 691
Camel Snus Frost Large	Appendix J, Page 694
Camel Snus Mint	Appendix H, Page 688
Camel Snus Winterchill	Appendix L, Page 697
Camel Snus Frost	Appendix G, Page 685

RAIS RESPONSE TO DEFICIENCY 8a

(b) (4)

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PM0000427- PM0000432/MR0000068-MR0000073 A/I PARTIAL RESPONSE – DEFICIENCY 8

(b) (4)



RAIS RESPONSE TO DEFICIENCY 8b

(b) (4)



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(b) (4)



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RAIS RESPONSE TO DEFICIENCY 8c

(b) (4)



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(b) (4)



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PM0000427- PM0000432/MR0000068-MR0000073 A/I PARTIAL RESPONSE – DEFICIENCY 8