RAI Services Company

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**CONFIDENTIAL, NOT FOR PUBLIC DISCLOSURE**

October 15, 2018

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 12) 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 Twelve (12) 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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RAI Services Company

FDA-Listed Deficiencies and RAIS Response

***12. For all your MRTPAs/PMTAs, you indicate that the in vitro sister chromatid exchange (SCE) assay was performed as per*** (b) (4) ***you referenced*** (b) (4) (b) (4) ***when describing the methods used in the SCE assay for preparing the Chinese hamster ovary (CHO-WBL) cell culture suspension, sister chromatid exchange staining and scoring, etc. However, the detailed protocol for*** (b) (4) ***test method could not be found in the application. A detailed description of all test methods and protocols used in the studies submitted in support of these MRTPAs/PMTAs is needed for a comprehensive toxicological review of the application. For all Camel Snus products that are the subject of these applications, provide the complete protocol*** (b) (4) ***referenced for the in vitro the sister chromatid exchange assay.***

RAIS RESPONSE

In Deficiency 12, FDA requests the complete protocol for (b) (4) referenced for the sister chromatid exchange assays submitted in the Camel Snus MRTPAs/PMTAs. (b) (4)