

3.3 Camel Snus Product Stability

Section 911(d)(3) of the TCA requires that applications for modified risk tobacco products include information regarding the “formulation of the tobacco product” ([TCA Section 911\(d\)\(3\)](#)). As one element of the formulation section of an application, FDA recommends that “data establishing the stability of the product through the stated shelf life” be included ([FDA MRTPA Draft Guidance 2012](#), p. 13). As such, this section summarizes information regarding Camel Snus product stability, including a summary description of RJRT’s manufacturing processes that promote stability and test results evaluating product stability.

Camel Snus does not have a shelf life, use-by date, or best-by date stated on the packaging. However, as part of making high quality products available to suppliers, retailers and consumers, there is a Wholesale Returned Goods Program with recommended stock rotation guidelines based on product age from the time of manufacture ([Wholesale Returned Goods Program](#)). For Camel Snus, RJRT’s program recommends that product be removed from a supplier warehouse after 11 months or from a retail outlet after 12 months and returned to the manufacturer.

Tobacco specific nitrosamines (TSNAs) are considered by many to be the most harmful toxicants present in smokeless tobacco ([IARC 2007b](#), p. 57). TSNA are formed by the nitrosation of alkaloids present in tobacco ([Brunnemann et al. 1996](#)). TSNA formation has been reported during curing, fermentation (for tobaccos processed in this manner) and aging of tobacco ([Brunnemann et al. 1996](#); [Fisher et al. 2012](#)). For tobaccos typically used in smokeless tobacco products, the mechanism of nitrosation involves the reduction of the nitrate content of tobacco, primarily by bacteria, leading to formation of nitrite which is a nitrosating agent ([Hoffmann et al. 2001](#); [Fisher et al. 2012](#)). Given this mechanism, RJRT conducted studies to assess the microbial activity and water activity of all Camel Snus brand styles that are the subjects of this Application, the moisture barrier properties of Camel Snus packaging, and the effects of aging a packaged Camel Snus style for one year under controlled conditions ([RDM JAH 2016,194](#); [RDM FKS 2016,221](#); [RDM FKS 2016,193](#)).

As described in detail in the following sections, RJRT studies show that Camel Snus is very stable with regards to microbial growth as a result of methods inherent in processing snus tobaccos. These processing methods include the application of salt (NaCl); heat treatment of the tobacco; the application of glycerin and/or propylene glycol; and drying to a water activity of ≤ 0.85 . Additionally, Camel Snus packaging has sufficient resistance to moisture transfer that there is low probability of Camel Snus gaining sufficient moisture during storage to promote microbial activity. Consistent with these facts, RJRT studies have shown TSNAs do not increase when Camel Snus is aged for an extended period. ([RDM FKS 2016,193](#)).

3.3.1 Camel Snus Processing and Product Stability

Processing tobacco via fermentation, a practice typical for smokeless tobacco products sold in the U.S., has been reported to result in higher TSNA concentrations than found for tobacco

processed via heat treatment techniques ([Österdahl et al. 2004](#)). Camel Snus is not fermented. Rather, Camel Snus is manufactured using a two-step heat treatment process, in order to impart the taste of the product, to reduce potential for microbial activity and to minimize potential for TSNA formation.

All Camel Snus styles are portioned pouched products that use a common blend of tobaccos. That tobacco blend is 60% tobacco lamina and 40% tobacco stem. It is first finely milled, subsequently mixed with water and salt, and then heat treated. After the initial heat treatment, a sodium carbonate and sodium bicarbonate pH-modifying solution is added to the tobacco and an additional heat treatment then occurs. In order to create differentiated flavor variants of Camel Snus, a humectant and unique flavoring ingredients are added to the processed common tobacco blend. The different flavor variants are then pouched in a porous fleece material and packaged in metal tins to make the finished product.

3.3.2 Microbial Stability

Camel Snus is very stable microbially. The manufacturing processes used by RJRT to produce Camel Snus creates multiple hurdles to avoid microbial proliferation ([Rahmann 2015](#)). These processes include the application of salt (NaCl), heat treatment of the tobacco to a target temperature of 202 °F for one hour, the application of glycerin and/or propylene glycol, and drying/maintaining the tobacco at a water activity of ≤ 0.85 .

Quarterly manufacturing audits over the period October 22, 2012 through April 12, 2016 indicated that Camel Snus products are microbiologically stable with very low potential for microbiological activity ([RDM JAH 2016,194](#)). All Camel Snus brands styles that are the subject of this Application were analyzed for total aerobic bacteria, total coliform bacteria, yeast, mold, and water activity. Coliform bacteria results for all 174 replicates representing all samples were less than the lower quantitation limit of 10 Colony Forming Units per gram (CFU/g). In addition, no colony forming units were found on any of the coliform bacteria plates. For yeast measurements, 99.4% of the replicates (173 of 174) were <10 CFU/g and the single replicate >10 was 13 CFU/g. For mold measurements, 98.3% of the replicates (171 of 174) were <10 CFU/g, and the three replicates greater than 10 were 17 CFU/g, or less. For the total aerobic bacteria, 70% of the replicates were <10 CFU/g. Even the highest value determined for any of the replicates (103 CFU/g) does not give a cause for concern because it is much lower than typical values reported for consumer goods such as processed spices and herbs ([Schwab et al. 1982](#)) or fermented tobacco ([Di Giacomo et al. 2007](#); [Han et al. 2016](#)).

The mean water activity (A_w) for Camel Snus Frost, Camel Snus Frost (Large), Camel Snus Mellow and Camel Snus Mint fell into the 0.82 to 0.83 range. The mean A_w for these 4 brands combined was 0.824 with a standard deviation of 0.0094. Among the 118 individual replicate A_w measurements for these 4 brand styles, only one had an A_w greater than 0.850. This was an A_w value of 0.857 for one replicate of Camel Snus Mint sampled on January 15, 2014 and the other Camel Snus Mint replicate on the same date was 0.830. The mean water activity for Camel Snus Robust and Camel Snus Winterchill were slightly lower than the other four brand styles, ranging from 0.75 to 0.76. These lower A_w measured value were probably due to slightly higher salt

(NaCl) content in these two brand styles. The overall mean for Camel Snus Robust and Winterchill was 0.757 with a standard deviation of 0.0096.

The packaging for the Camel Snus products was designed so that there would be minimal risk of product tampering, product contamination or significant change in water activity (RDM FKS 2016,221). The Camel Snus package is a two-piece tin-plated steel container. Because the steel is impermeable, the only route for contamination or moisture exchange is through the interface between the two pieces. The top piece (lid) has a rolled edge that snaps over 4 dimples on the bottom piece (base) to hold it closed. A bead of foamed plastisol is applied to the inside of the lid in an embossed channel. When the lid is applied to the base, the edge of the base presses into the plastisol bead to seal the interface between the two pieces and provide a barrier to contamination or water exchange. A shrink band is applied around the edge of the container to provide a tamper evident seal since the shrink band must be broken to open the package. Then a plastic sleeve is applied to a stack of 5 tins and is shrunk such that the edges of the plastic sleeve overlap the top and bottom edges of the stack, providing an additional protective barrier. The 5-tin sleeves are then placed in cardboard cases in two layers of nine sleeves which further protects against contamination. Using a resistance to moisture transfer (RDM FKS 2016,221) of 3×10^{-3} cc/day, it would take 125 days at 100 °F and 90% RH for the snus moisture in a single tin of 600 mg Camel Snus pouches to increase from 32% moisture to 33% moisture (135 mg moisture increase). For a 5-tin sleeve, estimated time for a 1% moisture increase lengthens to 225 days. These calculations demonstrate the low probability of Camel Snus gaining sufficient moisture during storage to promote microbial activity. After the tamper evident shrink band is removed by the consumer, the resistance to moisture transfer decreases by about 32% (RDM FKS 2016,221), but the tin still retains sufficient resistance to moisture transfer to provide ample moisture protection of the product during the use life.

Microbial stability was also demonstrated during a 12-month product stability study for Camel Snus Winterchill (RDM FKS 2016,193). For this study, total anaerobic bacteria were analyzed in addition to the microbial analyses used for the quarterly manufacturing audit. Anaerobic bacteria analysis was added to evaluate any effect of the plastisol seal. The product was stored in a controlled environment at a mean 75.7 °F and 60% relative humidity for the first ten months. Due to an equipment malfunction, for the last two months, the temperature was maintained in the mid-70 °F range by the normal air conditioning for the laboratory and the relative humidity was uncontrolled. For total anaerobic bacteria, coliform, mold and yeast, results were less than the quantitation limit of 10 colony forming units per gram (<10 CFU/g) for all samples measured over the 12-month period. For total aerobic bacteria, results were <10 CFU/g for all samples except for those from months eleven and twelve which were 95 and 26.5 CFU/g, respectively. Water activity declined slightly with a slope equivalent to $-0.0016 A_w$ unit/month. The moisture loss declined with a non-statistically significant (95% confidence level (C.L.)) slope of -0.085% moisture/month. This slope was less than, but comparable to, that predicted using the resistance to moisture transfer of 3×10^{-3} cc/day. Moisture was also measured on 5-pack sleeves as well as individual tins. A nominal, non-statistically significant (95% C.L.) slope of -0.056% moisture/month was found. A comparison of the data between

individual tins and 5-pack sleeves using a one-tailed paired t-test gave a non-significant p-value of 0.22.

3.3.3 Chemical Stability

During the 52 week product stability study for Camel Snus Winterchill ([RDM FKS 2016,193](#)), pH and tobacco specific nitrosamines (TSNA) were measured in addition to the microbial analysis, water activity and moisture discussed above. The TSNA's analyzed were N-nitrosonornicotine (NNN), N-nitrosoanatabine (NAT), N-nitrosoanabasine (NAB) and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK). Tobacco pH was measured monthly on product stored in individual tins and 5-pack sleeves. The slopes for a linear regression of pH versus time were statistically significant for both individual tins ($p=5.45 \times 10^{-4}$) and 5-pack sleeves ($p=1.09 \times 10^{-5}$) and were similar with a loss of about 0.02 pH units/month. The difference in the two sets of results was not statistically significant ($p=0.18$).

Total TSNA's (sum of the four individual TSNA concentrations) declined with a significant slope (95% CL) of about -12 ppb/month. For individual TSNA's, two significant slopes (95% CL) indicated declines of about -4.3 ppb/month for NNK and -7.4 ppb/month for NAT. Intercepts were 464 ppb and 430 ppb for NNK and NAT, respectively. NAB did not have a significant slope and NNN had no correlation with age ($R^2 \sim 0$). The mean concentrations for NNN and NAB were 1226 ppb and 78 ppb, respectively. The lack of an increase in TSNA's with product age is consistent with available information for other snus products which behaved similarly whether stored refrigerated, at room temperature or at elevated temperatures ([Brunnemann *et al.* 2001](#); [TPSAC Meeting, April 9, 2015](#) (Dr. Rutqvist); [TPSAC Meeting, April 10, 2015](#), (Dr. Lindholm); [Proctor and Sandi 2007](#)).

