

**7.5.8-1: INITIAL – TOPOGRAPHY - LITERATURE SUMMARY**

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**LIST OF ABBREVIATIONS**

BOE	Biomarkers of exposure
MRTPA	Modified Risk Tobacco Product Applications
MST	moist smokeless tobacco
NHANES	National Health and Nutrition Examination Survey
PD	pharmacodynamics
PK	pharmacokinetics
ST	smokeless tobacco
U.S.	United States

## **7.5.8-1. TOPOGRAPHY LITERATURE REVIEW**

### **7.5.8-1.1.Literature Summarizing How U.S. Consumers Use Smokeless Tobacco Products**

This section addresses the Food and Drug Administration's (FDA's) 2012 Modified Risk Tobacco Product Applications (MRTPAs) Draft Guidance recommendations for data and information on how consumers actually use tobacco products.

The FDA's MRTPA Draft Guidance (Section 6) recommends the data and information on how consumers actually use the tobacco product that is required for an MRTPA, and includes the following:

- “the number of units of the product consumed per day (e.g., cigarettes per day)”;
- “the way in which individuals consume each unit of the product (e.g., puffing profiles);
- “whether consumers can and are likely to comply with any instructions for product use”; and
- concurrent use of multiple products containing nicotine or tobacco.

Throughout this MRTPA, smokeless tobacco (ST) refers to the broad class of all United States (U.S.) smokeless tobacco products. Most of the available information related to how consumers use ST products is not product or product-class specific. Specific studies may refer to chewing tobacco, chew, snuff, moist snuff, snus, or smokeless tobacco in their assessments of how consumers use the products, but in very few cases is the product use assessment specific enough to determine with any certainty what ST product categories might be included. Nonetheless, in these few cases, they sufficiently describe how consumers use moist smokeless tobacco (MST) products. In the majority of the other cases the available research is relevant because MST products comprise a significant proportion of the ST products in the U.S. market for many years and the subject of this application is an MST product.

Altria Client Services LLC conducted a comprehensive literature search, through December 2014, to identify published information relevant to how consumers use ST products (Section 7.5.1 for a description of the review protocol and results). From this search, a total of 6,742 publications were identified, and, after a comprehensive and in depth critical review, 537 were determined to be in scope. These publications were further reviewed to assess which specific category(ies) in the MRTPA Draft Guidance each article addressed. Reports published shortly after the date of our last search were included in this review when deemed to be significant contributions to this body of research. This literature search yielded 73 publications describing how U.S. consumers use ST products, thus providing relevant information addressing the issues posed by the FDA's MRTPA 2012 Draft Guidance.

An updated literature review was conducted to bridge the original review to February 2017, and updated findings that inform topography are presented in Section 7.5.8-2.

### **7.5.8-1.2.Characteristics of Studies Published in the Scientific Literature of How U.S. Consumers Use Smokeless Tobacco Products**

The publications reporting how consumers use ST products span a wide range of characteristics. Consequently, a wide range of findings have been reported for how consumers use ST products. Study methods include surveys, interviews, questionnaires, clinical trials, longitudinal studies, field studies, and secondary analyses of data from nationally representative surveys. The number of subjects evaluated in the publications reviewed ranged from as few as 8 (Benowitz, Jacob III, & Yu, 1989) to as many as 31,145 (Grier, Knapik, Canada, Canham-Chervak, & Jones, 2010). Participants in these studies included school-age adolescents, Native Americans, college students, college athletes, military personnel, professional athletes, and males and females of the general public. The products most commonly evaluated were described as smokeless tobacco, snuff, or chewing tobacco.

Some of the publications reviewed had either presented a relatively large number of measures of ST use behaviors, or had stated an objective of assessing ST use patterns (Ary, Lichtenstein, & Severson, 1987; Boyle, Gerend, Peterson, & Hatsukami, 1998; Boyle, Jensen, Hatsukami, & Severson, 1995; Cohen-Smith & Severson, 1999; Colborn, Cummings, & Michalek, 1989; Ebbert, Severson, Danaher, Schroeder, & Glover, 2012; Ernster et al., 1990; Hatsukami, Anton, Callies, & Keenan, 1991; Hatsukami, Jensen, Boyle, Grillo, & Bliss, 1999; Hatsukami, Keenan, & Anton, 1988; Lemmonds et al., 2005; Marty, McDermott, & Williams, 1986; Mushtaq, Beebe, & Vesely, 2012; Oliver, Jensen, Vogel, Anderson, & Hatsukami, 2013; Riley, Barenie, & Myers, 1989; Rodu, Plurphanswat, & Fagerstrom, 2014; Severson, Eakin, Lichtenstein, & Stevens, 1990; Wisniewski & Bartolucci, 1989). Other studies had different objectives, such as measuring demographics, exposure, health effects, dependence, etc., but also included some relevant measurements of usage characteristics to support results from the primary objectives. Findings from this latter group of studies were typically similar to findings from the more focused topography and use pattern studies. Characteristics and findings from the 73 studies presenting findings of typical use patterns are presented in Table 7.5.8-1-2 and Table 7.5.8-1-3. Table 7.5.8-1-3 summarizes literature related to misuse of tobacco products.

### **7.5.8-1.3.How U.S. Consumer Smokeless Tobacco Product Actual Use Characteristics**

Quantitative measures of how consumers actually use ST products have been presented in many studies published in the scientific literature. Characteristics and findings of these studies are presented in Table 7.5.8-1-2.

The most frequently reported measure is cans, sometimes referred to as tins, used per week. Some investigators use the number of days a can of ST lasts, and this measure can be converted to cans per week by calculation. Other measures frequently used to characterize ST use, include dips per day, average dip size, average time a single dip is held in the mouth, and total hours per day that dip is used. Findings for the more frequently reported measures of ST use are presented in Table 7.5.8-1-1.

**Table 7.5.8-1-1: Common Measures and Values of Smokeless Tobacco Use**

Product Use Measure	Value	Source
Cans per week		
Mean	3.7	(Hatsukami et al., 1999)
Range	1-22	(Hatsukami et al., 1999)
Dips per day		
Mean (male)	7.6	(Cohen-Smith & Severson, 1999)
SD (male)	4.7	(Cohen-Smith & Severson, 1999)
Mean (female)	6.0	(Cohen-Smith & Severson, 1999)
SD (female)	4.9	(Cohen-Smith & Severson, 1999)
Dip size (g)		
Mean	1.2	(Severson et al., 1990)
Range	0.1-7.3	(Severson et al., 1990)
Duration of use, single dip (min)		
Mean	39.9	(Hatsukami et al., 1988)
Range	13.9-83.9	(Hatsukami et al., 1988)
Duration dip is held in the mouth per day (min)		
Mean	283.5	(Hatsukami et al., 1991)
Range	79.7-757.1	(Hatsukami et al., 1991)

In addition to the more frequently reported measures of ST use, other, measures have been reported characterizing how consumers use smokeless tobacco products.

- The percentage of people who intentionally swallow the juice of smokeless tobacco products was reported to be: never, 33% (33 of 100); sometimes, 47% (47 of 100); and always, 20% (20 of 100) (Boyle et al., 1995).
- About 8.4% (20 of 237) of people report leaving dip in their mouth overnight (Ferketich, Wee, Shultz, & Wewers, 2007).
- 61% (61 of 100) and 60% (135 of 224) of smokeless tobacco consumers surveyed reported they keep a dip in their mouth almost all the time (Boyle et al., 1995; Ebbert et al., 2012).

In one study, 11.3% (6 of 53) of the subjects reported using two or more pouches simultaneously (Caraway & Chen, 2013).

Moist snuff products currently commercially available in the United States, including this MRTP, do not have instructions for use. Therefore, relevant information was not found in the published scientific literature.

Concurrent use of smokeless tobacco products with other tobacco products is addressed in Section 7.5.2-1 and Section 7.5.2-2 of this MRTPA.

#### **7.5.8-1.4.Misuse of Tobacco Products**

Misuses of tobacco products have been reported. Examples include making concentrated extracts of tobacco to use as folk remedies for various health conditions (Garcia-Estrada & Fishman, 1977; O'Berst & McIntyre, 1953; Willis, 1937) or for intentionally committing suicide (Schneider et al., 2010). Accidental ingestion of tobacco products, including ST, is a potential hazard for very young children (Smolinske et al., 1988). Research has indicated that serious outcomes from such occurrences are relatively rare (Appleton, 2011).

Characteristics and outcomes of studies cited in this section are presented in Table 7.5.8-1-3.

#### **7.5.8-1.5.Summary and Conclusions**

The FDA's MRTPA Draft Guidance (Section 6) recommends the data and information on how consumers actually use the tobacco product that is required for an MRTPA, and includes the following:

- “the number of units of the product consumed per day (e.g., cigarettes per day)”;
- “the way in which individuals consume each unit of the product (e.g., puffing profiles);
- “whether consumers can and are likely to comply with any instructions for product use”; and
- concurrent use of multiple products containing nicotine or tobacco.

The available published literature indicates the average consumer of MST uses 7 to 8 dips per day, and 3 to 4 cans per week. An average dip size is between 1 and 2 g. An average dip lasts 40 to 50 minutes, and over an entire day, a user keeps dip in their mouth an average of 5 to 6 hours.

Although the potential for misuse is possible, historical experience indicates that the frequency of such events being associated with severe outcomes is relatively rare.

Moist snuff products commercially available in the United States, including this MRTP, do not have instructions for use. Therefore, relevant information was not found in the literature search.

Concurrent use of smokeless tobacco products with other tobacco products is addressed in Section 7.5.2-1 and Section 7.5.2-2 of this MRTPA.

**Table 7.5.8-1-2: Literature Evaluating How Consumers Use Smokeless Tobacco Products**

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Jitnarin, Poston, Haddock, Jahnke, & Day, 2015)	Tobacco use pattern among a national firefighter cohort	Cohort study, ST, 947 male firefighters, age mean (SD) = 39.1 (8.8).	Mean (SD) = 2.8 (SD = 2.8) tins/wk	Mean (SD) = 4.0 (3.6) dips per day.	Not included in article.	Not included in article.	Not included in article.	Limitation = unique sample population may not be generalizable
(Rodu et al., 2014)	Time to first use among daily smokers and smokeless tobacco users	Secondary analysis of data from the Tobacco Use Supplement of the Current Population Survey, 1,176 ST consumers, average age 48 years.	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Time to first dip: • Within 5 min = 10% • Within 30 min = 29%	Strength = study specifically designed to assess time to first dip, limitation = only one topographical measure conducted.
(Liu et al., 2014)	Adolescent and adult perceptions of traditional and novel smokeless tobacco products and packaging in rural Ohio	Focus groups and qualitative interviews, male ST consumers from rural Ohio counties; 23 adolescents with mean age 17 years, 38 adults with mean age 29 years.	≤1 • Adolescents: 13.0% • Adults: 18.4% 2-4 • Adolescents: 47.8% • Adults: 50.0% ≥5 • Adolescents: 26.1% • Adults: 31.6%	Not included in article.	Not included in article.	Not included in article.	Time to first dip of the day: Adolescents: • >30 min = 73.9% • <30 min = 21.7% Adults: • >30 min = 65.8% • <30 min = 34.2% Frequency in days per week: ≤5 • Adolescents: 43.5% • Adults: 34.2% 6-7 • Adolescents: 43.5% • Adults: 65.8%	Strength = good selection of topographical measures, limitation = small sample size.

<sup>1</sup> One can contains 34.02 g of loose snuff, 23.45 g of pouched snuff

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Oliver et al., 2013)	Flavored and non-flavored smokeless tobacco products: rate, pattern of use, and effects	Analysis of data from 5 previously treatment or switching studies, 468 subjects, mean age (SD) in no-flavor group = 37.3 (7.7), in flavor group = 32.5 (7.8).	Mean (SD)• No-flavor group = 4.0 (2.4)• Flavor group = 3.9 (2.0)	Mean (SD)• No-flavor group = 9.9 (5.7)• Flavor group = 8.8 (5.3)	Not included in article.	Hours, mean (SD)• No-flavor group = 12.2 (7.5)• Flavor group = 11.8 (7.2)	Not included in article.	Strengths = includes some unique topographical measures.
(Caraway & Chen, 2013)	Assessment of mouth-level exposure to tobacco constituents in U.S. snus consumers	Assessment of mouth level constituent exposure, 53 adult snus consumers, aged 21-55 years.	Not included in article.	Not included in article	<ul style="list-style-type: none"> <li>• &lt;10 = 26.4%</li> <li>• 10-30 = 50.9%</li> <li>• &gt;30 = 26.4%</li> </ul>	Not included in article.	<ul style="list-style-type: none"> <li>• 6 (11.3%) of the subjects reported using two or more pouches simultaneously.</li> <li>• 51% reported they moved the pouch around in the mouth during use.</li> </ul>	Limitation = small sample size.
(Danaher et al., 2013)	Randomized controlled trial of MyLastDip: a Web-based smokeless tobacco cessation program for chewers ages 14-25	Interactive web-based cessation tool, ST, 1,716 participants, aged 14-25 years.	<ul style="list-style-type: none"> <li>• &lt;1 = 0.1%</li> <li>• 1-2 = 28.8%</li> <li>• 3-4 = 36.9%</li> <li>• ≥5 = 34.2%</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = tobacco abstinence not verified biochemically.
(Ebbert, Severson, Croghan, Danaher, & Schroeder, 2013)	Comparative effectiveness of the nicotine lozenge and tobacco-free snuff for smokeless tobacco reduction	Multi-center, randomized clinical pilot study, 81 ST consumers undergoing cessation treatment, average age 37.8 years.	<ul style="list-style-type: none"> <li>• Baseline for control group, mean (SD) = 3.2 (2.1)</li> <li>• Baseline for intervention group, mean 4.0 (2.7)</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline for control group, mean (SD) = 7.6 (4.2)</li> <li>• Baseline for intervention group, mean (SD) = 9.7 (3.7)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Strengths/limitations = none noted.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Jitnarin, Haddock, Poston Walker, & Jahnke, 2013)	Smokeless tobacco and dual use among firefighters in the central United States	Longitudinal cohort study, ST, 353 male career firefighters, mean age (SD) = 39.4 (10.1) years.	Not included in article.	<ul style="list-style-type: none"> <li>• Among exclusive ST consumers, mean (SD) = 4.9 (3.3)</li> <li>• Among dual consumers, mean (SD) = 2.7 (2.9)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Limitations = unique sample population may not be generalizable and few topographical measures.
(Ebbert et al., 2012)	A comparison of three smokeless tobacco dependence measures	Secondary analysis from clinical trial, 225 ST consumers, aged 19-72 years.	Not included in article.	<ul style="list-style-type: none"> <li>• 1-9 = 50%</li> <li>• 10-15 = 39%</li> <li>• &gt;15 = 10%</li> </ul>	<ul style="list-style-type: none"> <li>• 10-19 = 9%</li> <li>• 20-30 = 22%</li> <li>• &gt;30 = 69%</li> </ul>	Not included in article.	<ul style="list-style-type: none"> <li>• 60% said they keep a dip in their mouth almost all the time.</li> <li>• Swallow the juice: never = 25%; sometimes = 45%; always = 30%</li> </ul>	Strengths = large sample and some unique topography measures.
(Mushtaq et al., 2012)	Determinants of salivary cotinine concentrations among smokeless tobacco users	Survey, 95 current adult ST consumers, mean (SD) age 31.9 (12.2).	Mean (SD) = 3.6 (2.2)	Mean (SD) = 6.6 (4.5)	Not included in article.	Not included in article.	Swallow juice: Yes = 46.3% No = 53.7%	Strengths = relatively good selection of topographical measures.
(Benowitz et al., 2012)	Exposure to nicotine and carcinogens among Southwestern Alaskan Native cigarette smokers and smokeless tobacco users	Survey of tobacco use history and BOEs, Alaskan Natives, 76 ST consumers, 20 Iqmik consumers, 31 dual consumers, aged 18 years and older.	“Average” <ul style="list-style-type: none"> <li>• ST = 1.6</li> <li>• Iqmik = 1.2</li> <li>• Dual consumers = 1.3</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.
(Schiller et al., 2012)	Comparing an immediate cessation versus reduction approach to smokeless tobacco cessation	Intervention study, 199 ST consumers, mean age (SD) 34.8 (8.5) years.	<ul style="list-style-type: none"> <li>• Immediate cessation mean (SD) = 3.5 (3.1)</li> <li>• Brand switching mean (SD) = 3.9 (1.7)</li> <li>• Nicorette Lozenge mean (SD) = 3.4 (3.4)</li> </ul>	<ul style="list-style-type: none"> <li>• Immediate cessation mean (SD) = 7.5 (6.9)</li> <li>• Brand switching mean (SD) = 8.2 (3.0)</li> <li>• Nicorette Lozenge mean (SD) = 6.9 (2.5)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Strengths/limitations = none noted.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Ebbert, Severson, Croghan, Danaher, & Schroeder, 2010)	A pilot study of mailed nicotine lozenges with assisted self-help for the treatment of smokeless tobacco users	Clinical pilot study randomizing 60 ST consumers undergoing cessation treatment.	<ul style="list-style-type: none"> <li>• Placebo group, mean (SD) = 3.7 (2.1)</li> <li>• Nicotine lozenge group, mean (SD) = 3.9 (2.1)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = limited number of topographical measurements.
(Ebbert, Croghan, North, & Schroeder, 2010)	A pilot study to assess smokeless tobacco use reduction with varenicline	Pilot study, 20 male ST consumers undergoing cessation treatment, mean age (SD) 42.8 (11.7) years.	Mean (SD) = 3.9 (1.7) (range, 2-7)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = small sample size.
(Ebbert, Edmonds, Luo, Jensen, & Hatsukami, 2010)	Smokeless tobacco reduction with the nicotine lozenge and behavioral intervention	Behavioral intervention study, 102 ST consumers, mean age 35 years.	Mean (SD) = 4.3 (1.9)	Mean (SD) = 10.1 (5.2)	Not included in article.	Not included in article.	Not included in article.	Limitation = limited topographical measures.
(Grier et al., 2010)	Tobacco use prevalence and factors associated with tobacco use in new U.S. Army personnel	Questionnaire, military students, 27,289 men and 3,856 women, aged 17-24 years (mean age (SD), 20 (2) years).	<ul style="list-style-type: none"> <li>• &lt;1 can/d = 63%</li> <li>• 1 can/d = 31%</li> <li>• ≥2 cans/d = 5%</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = limited topographical measures.
(Walsh et al., 2010)	Smokeless tobacco cessation cluster randomized trial with rural high school males: intervention interaction with baseline smoking	Stratified randomized controlled trial, 4,731 male high school students.	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Time to first dip: <ul style="list-style-type: none"> <li>• Among dual consumers = 40% within 30 min of waking</li> <li>• Among exclusive ST consumers = 22% within 30 min or waking</li> </ul>	Limitation = poor reporting of topography data.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Ebbert, Severson, Croghan, Danaher, & Schroeder, 2009)	A randomized clinical trial of nicotine lozenge for smokeless tobacco use	Randomized Clinical trial, 270 ST consumers, average age 36.5 years.	Mean (SD) = 4.2 (2.6)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = limited number of topographical measures.
(Gillum, Obisesan, & Jarrett, 2009)	Smokeless tobacco use and religiousness	Secondary analysis of data from NHANES survey, smokeless tobacco, 9,374 men, aged ≥17 years.	Median = 3.0	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = possible bias from nonresponse and missing data for some variables.
(Severson et al., 2009)	Smokeless tobacco cessation in military personnel: a randomized controlled trial	Randomized control trial, 785 active-duty military personnel, mean age (SD) 30.4 (7.6) years.	1.9 (calculated)	Not included in article.	Not included in article.	Not included in article.	<ul style="list-style-type: none"> <li>• Time to first dip: Percentage within 30 min = 23.9%</li> <li>• Number of days a can lasts: Mean (SD) = 3.7 (2.2)</li> <li>• Use of ST, days/wk: Mean (SD) = 6.2 (1.5)</li> </ul>	Limitation = unique population may not be generalizable.
(Hatsukami et al., 2008)	Smokeless tobacco reduction: preliminary study of tobacco-free snuff versus no snuff	12-week intervention study, 106 ST consumers, age mean (SD) = 33.7 (7.3).	<ul style="list-style-type: none"> <li>• Treatment group, mean (SD) = 4.2 (1.7)</li> <li>• Control group, mean (SD) = 4.2 (1.8)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.
(Hecht, Carmella, Edmonds, et al., 2008)	Exposure to nicotine and a tobacco-specific carcinogen increase with duration of use of smokeless tobacco	Questionnaires, 212 male smokeless tobacco consumers, mean age 33.8 (95% CI 32.8-34.8) years.	Average = 4.2 (95% CI 3.9-4.4)	Average = 9.9 (95% CI 9.1-10.6)	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Hecht, Carmella, Stepanov, et al., 2008)	Metabolism of the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone to its biomarker total NNAL in smokeless tobacco consumers	Estimation of NNK dose following use of ST, 15 male subjects, mean age (SD) 32.2 (6.1) years.	Mean (SD) 1.1 (0.8) (range, 0.3-3.5)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = small sample size and few topographical measures
(Ferketich et al., 2007)	Smokeless tobacco use and salivary cotinine concentration	Survey plus clinical measures, 256 male smokeless tobacco consumers (87.9% snuff only, 9% chew only, 3.1% snuff + chew) living in the Ohio Appalachian region (86.7% lived in the Appalachian region until age 18), average age 34 years.	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Time between dips: • ≤30 min = 45.3% • >30 min = 54.7% Leave dip in overnight: • Yes = 8.4% • No = 91.6%	Limitation = few topographical measures.
(Hatsukami et al., 2007)	Smokeless tobacco brand switching: a means to reduce toxicant exposure?	Study examined the effects of ST brand switching on biomarkers of exposure and on ST use, 66 subjects interested in reducing ST use but not quitting, mean age 31.8 years (ad libitum group).	Tins/wk, mean (SE) = 4.2 (1.9) for ad libitum group	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = most topographical measures reported as correlations with other parameters and absolute values not presented

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Hecht et al., 2007)	Similar exposure to a tobacco-specific carcinogen in smokeless tobacco consumers and cigarette smokers	Comparison of NNK exposure among ST vs. cigarette consumers, 420 smokers and 182 smokeless tobacco consumers, mean age 32.9 years (95% CI, 31.9-33.9).	Average tins/wk = 4.2 (95% CI, 3.9-4.4).	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = few topographical measures.
(Peterson et al., 2007)	Smokeless tobacco use in military personnel	Baseline assessment for randomized clinical trial, 785 active duty U.S. Military personnel, average age (SD) 30.4 years (7.63).	Not included in article.	Not included in article.	Not included in article.	Not included in article.	<ul style="list-style-type: none"> <li>• Number of days a can lasts Mean (SD) = 3.7 (2.16)</li> <li>• Time to first dip percentage less than 30 min = 23.9</li> <li>• Swallows spit = 49.9%</li> </ul>	Strengths = study presents some novel topographical measures.
(Thomas et al., 2006)	Measuring nicotine dependence among smokeless tobacco users	Randomized, double-blind, placebo-controlled pilot study, 68 adult ST consumers, median age 32 years (range, 24-72 years).	<ul style="list-style-type: none"> <li>• ≤2 = 31%</li> <li>• &gt;2-4 = 39%</li> <li>• 4+ = 31%</li> </ul>		Mean (SD) = 82.9 (131.9)	In hours: <ul style="list-style-type: none"> <li>• ≤14.5 = 33%</li> <li>• 14.5-15.5 = 31%</li> <li>• &gt;15.5 = 36%</li> </ul>	Time to first dip: <ul style="list-style-type: none"> <li>• 0-30 min = 42%</li> <li>• &gt;30 min = 58%</li> </ul> Swallow juice? How often: <ul style="list-style-type: none"> <li>• Never = 31%</li> <li>• Sometimes = 25%</li> <li>• Always = 44%</li> </ul>	Strength = large number of topographical measures, limitation = most of the participants were seeking cessation treatment.
(Lemmonds et al., 2005)	Smokeless tobacco topography and toxin exposure	Measurement of ST topographical measures and biomarkers of exposure. 54 male participants, mean age (SD) 32.1 (7.5) years.	Mean (SD) = 3.4 (2.8)	Mean (SD) = 6.8 (3.0)	Mean (SD) = 71.2 (44.3)	Minutes, mean (SD) = 423.0 (224.4)	Not included in article.	Strengths = study designed to be a topography study.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Ebbert et al., 2005)	A survey of characteristics of smokeless tobacco users in a treatment program	Survey, 162 patients for ST use, average age 44.5 years.	<ul style="list-style-type: none"> <li>• ≤3 cans/wk = 79%</li> <li>• ≥4 cans/wk = 22%</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.
(Ebbert, Dale, Nirelli, et al., 2004)	Cotinine as a biomarker of systemic nicotine exposure in spit tobacco users	Intervention trial, 68 daily ST consumers, mean age (SD) 36.5 (12.5) years.	<ul style="list-style-type: none"> <li>• Mean (SD) = 3.3 (2.1)</li> <li>• Median = 3.0 (range, 1-11)</li> </ul>	<ul style="list-style-type: none"> <li>• Mean (SD) = 12.8 (10.2)</li> <li>• Median = 10 (range, 3-70)</li> </ul>	<ul style="list-style-type: none"> <li>• Mean (SD) = 82.9 (131.9)</li> <li>• Median = 45 (range, 10-930)</li> </ul>	Not included in article.	<b>Swallow juice:</b> never = 29% sometimes = 32% always = 38%	Strengths/limitations = none noted.
(Ebbert, Dale, Vickers, et al., 2004)	Residential treatment for smokeless tobacco use: a case series	Residential treatment program, 24 ST consumers, mean participant age (SD) = 47.4 (18.2) years.	<ul style="list-style-type: none"> <li>• Mean (SD) = 4.4 (2.6),</li> <li>• Median = 3.5 (range, 1.0-10.5)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = limited topographical measures.
(Spangler, Case, Bell, & Quandt, 2003)	Tobacco use in a tri-ethnic population of older women in southeastern North Carolina	Survey, ST, 240 women, aged 60 or older.	Not included in article.	Mean (SD)= 3.1 (1.7) (range, 0.07-8.00)	Not included in article.	Not included in article.	Not included in article.	Limitations = few topographical measures and unique population may not be generalizable.
(Wetter et al., 2002)	Concomitant use of cigarettes and smokeless tobacco: prevalence, correlates, and predictors of tobacco cessation	Longitudinal study (4-year follow-up); smokeless tobacco; 567 ST consumers, mean age 35.9 years; 115 dual consumers, mean age 35.5 years.	Not included in article.	<ul style="list-style-type: none"> <li>• ST consumers = 7.6</li> <li>• Dual consumers = 5.0</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Strength = longitudinal design; limitations = more dual consumers lost to follow up vs. ST-only consumers.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Dale et al., 2002)	Bupropion for the treatment of nicotine dependence in spit tobacco users: a pilot study	Randomized, double-blind, placebo-controlled pilot study, "spit" tobacco, 68 adult ST consumers.	Mean (SD) (range) <ul style="list-style-type: none"> <li>• Placebo group: 3.5 (2.4) (range, 1-11)</li> <li>• Intervention group: 3.1 (1.9) (range, 1-8)</li> </ul>	Mean (SD) (range) <ul style="list-style-type: none"> <li>• Placebo group: 11.8 (6.9) (range, 3-34)</li> <li>• Intervention group: 14.7 (12.9) (range, 4-70)</li> </ul>	Mean (SD) (range) <ul style="list-style-type: none"> <li>• Placebo group: 64.7 (60.0) (range, 10-270)</li> <li>• Intervention group: 101.2 (176.0) (range, 15-930)</li> </ul>	Not included in article.	Not included in article.	Limitation = small sample size.
(Hecht et al., 2002)	Quantitation of metabolites of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone after cessation of smokeless tobacco use	Quantitation of NNK metabolites following ST use, 13 male nonsmokers, 11 snuff dippers, 2 tobacco chewers, mean age (SD) 39.5 (10.7) years.	Mean (SD) = 3.4 (1.9) (range, 1-8)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = small sample size and few topographical measures.
(Andrews, Severson, Akers, Lichtenstein, & Barckley, 2001)	Who enrolls in a self-help cessation program for smokeless tobacco?	ST cessation trial, among random digit dialing sample, 222 participants, age 36.4 years.	Random digit dialing sample = 3.0 tins/wk	Not included in article.	Not included in article.	Not included in article.	Among self-help sample: • Tins/wk = 4.2 • Chew within 30 min of waking = 58.6% • Swallow juice = 74.1%	Strength = large sample size, limitation = none noted.
(Spangler et al., 2001)	Dual tobacco use among Native American adults in southeastern North Carolina	Telephone survey, ST, 400 adult Lumbee Indians in Pembroke, North Carolina, average age of ST consumers = 57 years.	Not included in article.	<ul style="list-style-type: none"> <li>• ST only = 3.6 (0.3)</li> <li>• Dual consumers = 5.2 (1.4)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Limitation = unique population may not be generalizable.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Cohen-Smith & Severson, 1999)	A comparison of male and female smokeless tobacco use	Interviews, 59 male and 51 female ST consumers from the Pacific Northwest, aged 18-71 years.	Not included in article.	<ul style="list-style-type: none"> <li>Men, mean (SD) = 7.6 (4.7)</li> <li>Women, mean (SD) = 6.0 (4.9)</li> </ul>	<ul style="list-style-type: none"> <li>Men, mean (SD) = 63.3 (65.8)</li> <li>Women, mean (SD) = 47.0 (45.0)</li> </ul>	Men average 481.1 min/d Women average 282 min/d	Not included in article.	Limitations = convenience sample not generalizable and demographics not well matched between male and female subjects.
(Hatsukami et al., 1999)	Characteristics of smokeless tobacco users seeking treatment	Questionnaire, 402 smokeless tobacco consumers seeking treatment, mean (SD) age 30.8 (8.7) years.	Average (SD) = 3.7 (2.5) (range, 1-22)	Average (SD) = 10.6 (6.1) (range, 1-56)	Mean (SD) = 46.5 (34.9) (range, 7-240)	Mean (SD) = 8.9 h (5.0) (range, 1-24)	Not included in article.	Strengths = large sample size and many topographical measures.
(Fant, Henningfield, Nelson, & Pickworth, 1999)	Pharmacokinetics and pharmacodynamics of moist snuff in humans	PK study, 10 male moist snuff consumers, average age 32.2 years (range, 26-45 years).	Not included in article.	Mean = 6.4 (range, 3-12)	Not included in article.	Not included in article.	Not included in article.	Limitations = small sample size and limited topographical measures.
(Boyle et al., 1998)	Use of smokeless tobacco by young adult females	Questionnaire and interview, 20 women ST consumers, aged 19-39 years.	Not included in article.	Mean (SD) = 3.6 (3.0)	Mean (SD) = 22.5 (9.6)	Not included in article.	Mean dip weight = 1.64 g (range, 0.2-4.6 g)	Limitations = small sample size limited to women.
(McChargue & Collins, 1998)	Differentiating withdrawal patterns between smokers and smokeless tobacco users	Comparison of withdraw symptoms between ST consumers and smokers, 19 male undergraduate students, age range 18-21 years.	Mean (SD) = 2.9 (1.0) tins/wk	Mean (SD) = 4.7 (1.2) dips/d	Not included in article.	Not included in article.	Not included in article.	Limitation = small sample size.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Hannam, 1997)	Smokeless tobacco use among Big Ten wrestlers and selected associated factors	Questionnaire, ST, 234 Big Ten intercollegiate wrestlers.	In season: <ul style="list-style-type: none"> <li>• &lt;1 can/wk = 30.8%</li> <li>• &gt;5 cans/wk = 10.8%</li> </ul> Off-season: <ul style="list-style-type: none"> <li>• &lt;1 can/wk = 33.3%</li> <li>• &gt;5 cans/wk = 12.1%</li> </ul>	Not included in article.	>30 = 19%	Not included in article.	Not included in article.	Limitation = unique sample may not be generalizable.
(Riley et al., 1996)	Adult smokeless tobacco use and age of onset	Semi-structured interviews, 345 current adult ST consumers, average age (SD) 29.4 years (13.0).	Not included in article.	<ul style="list-style-type: none"> <li>• &lt;12 years old = 5.96</li> <li>• 12-18 years old = 5.36</li> <li>• &gt;18 years old = 7.28</li> </ul>	Not included in article.	Not included in article.	Frequency of use per day: <ul style="list-style-type: none"> <li>• Snuff consumers = 6</li> <li>• Chewing tobacco consumers = 4.5</li> </ul>	Limitation = limited topographical measures.
(Boyle et al., 1995)	Measuring dependence in smokeless tobacco users	Cross-sectional clinical survey of ST consumers, Sample 1 = 100 ST consumers in Oregon (average age = 32 ± 10.5 years), Sample 2 = 121 male ST consumers in Minnesota, average age (SD) 31 (9.2) years.	Sample 2: <ul style="list-style-type: none"> <li>• ≤2 = 34.7%</li> <li>• &gt;2 = 36.4%</li> <li>• ≥4 = 28.9%</li> </ul>	Sample 1: <ul style="list-style-type: none"> <li>• 1-9 = 39%</li> <li>• 10-15 = 46%</li> <li>• &gt;15 = 15%</li> </ul>	Sample 1: <ul style="list-style-type: none"> <li>• 10-19 = 22%</li> <li>• 20-30 = 27%</li> <li>• &gt;30 = 51%</li> </ul>	Sample 2: <ul style="list-style-type: none"> <li>• ≤14.5 h = 37%</li> <li>• &gt;14.5 h = 31.5%</li> <li>• &gt;15.5 h = 31.5%</li> </ul>	Sample 1: Do you keep a dip or chew in your mouth almost all the time? <ul style="list-style-type: none"> <li>• Yes = 61%</li> <li>• No = 39%</li> </ul> Swallow juice? <ul style="list-style-type: none"> <li>• Never = 33%</li> <li>• Sometimes = 47%</li> <li>• Always = 20%</li> </ul> Sample 2: <ul style="list-style-type: none"> <li>• Never = 30.6%</li> <li>• Sometimes = 49.6%</li> <li>• Always = 19.8%</li> </ul>	Strengths = large sample sizes and large number of topographical measures.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Tilashalski, Lozano, & Rodu, 1995)	Modified tobacco use as a risk-reduction strategy	Interviews, 22 adult ST consumers, mean age 49.4 years (range, 27-77 years).	Average = 5.3	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = small sample size and few topographical measures.
(Lopez & Sanchez-Rico, 1994)	Smokeless tobacco consumption by Mexican-Americans and Anglo-Americans in southwestern New Mexico	Telephone survey; ST; 210 participants; average ages Anglo-American males = 41, Anglo-American females = 52, Mexican American males = 31, Mexican American females = 45.	<ul style="list-style-type: none"> <li>• Among Anglo-American male snuff dippers, “modal” amount = 2 cans/wk</li> <li>• Among Mexican-American snuff dippers, “modal” amount = 3 cans/wk</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = poor data presentation format.
(Baldini, Skinner, Landers, & O'Connor, 1992)	Effects of varying doses of smokeless tobacco at rest and during brief, high-intensity exercise	PK-PD study, 12 adult male snuff consumers, aged 18-29 years.	<ul style="list-style-type: none"> <li>• Heavy consumers, mean (SD) = 4.5 (2.0)</li> <li>• Light consumers, mean (SD) = 1.8 (1)</li> </ul>	<ul style="list-style-type: none"> <li>• Heavy consumers, mean (SD) = 8 (2.4)</li> <li>• Light consumers, mean (SD) = 6 (4)</li> </ul>	Not included in article.	Not included in article.	Mean dip size, g: <ul style="list-style-type: none"> <li>• Heavy consumers, mean (SD) = 2.15 (0.37)</li> <li>• Light consumers, mean (SD) = 1.38 (0.46)</li> </ul>	Limitation = small sample size.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Hatsukami, Anton, Keenan, & Callies, 1992)	Smokeless tobacco abstinence effects and nicotine gum dose	Randomized double blind clinical study, male ST consumers, N = 23 in Experiment 1 and N = 79 in Experiment 2, all college students.	Experiment 1, mean (SD): <ul style="list-style-type: none"> <li>• Group 1: 2.4 (0.8)</li> <li>• Group 2: 3.1 (2.5)</li> </ul> Experiment 2, mean (SD): <ul style="list-style-type: none"> <li>• Group 1: 2.6 (1.3)</li> <li>• Group 2: 2.6 (2.0)</li> <li>• Group 3: 2.4 (0.7)</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.
(Sinusas, Coroso, Sopher, & Crabtree, 1992)	Smokeless tobacco use and oral pathology in a professional baseball organization	Survey plus clinical examinations, smokeless tobacco and chewing tobacco, 206 professional baseball players, average age 25.4 years (range, 17-58 years).	<ul style="list-style-type: none"> <li>• 2.35 during season</li> <li>• 1.72 off season</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = few topographical measures and unique population may not be generalizable.
(Hatsukami et al., 1991)	Situational factors and patterns associated with smokeless tobacco use	Survey, 30 male smokeless tobacco consumers, mean (SD) age 20.5 (2.3) years.	Not included in article.	Mean (SD) = 7.2 ( 2.5) (range, 2.4-13.4)	Mean (SD) = 39.6 (18.3) (range, 19.1-106.0)	Mean (SD) = 283.5 (149.2) (range, 79.7-757.1)	<ul style="list-style-type: none"> <li>• Dip size = dry weight, after use: mean (SD) = 0.75 g (0.57) (range, 0.13-3.12 g)• Interdip interval mean (SD) = 71.2 min (32.2) (range, 21.3-145.7 min)</li> </ul>	Strength = large set of topographical measures, limitation = small sample size.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Tolbert, Shy, & Allen, 1991)	Micronuclei and other nuclear anomalies in buccal smears: a field test in snuff users	Field micronucleus test in 38 female snuff consumers and 15 female nonconsumers, age mean (SD) in snuff consumers 63.2 (13.1) years, age mean (SD) in snuff nonconsumers = 61.4 (15.0) years.	Mean (SD) = 1.7 (1.5) (range, 0.25-7)	Mean (SD) = 3.6 (1.6) (range, 0.7-8)	Mean (SD) = 125 (117) (range, 3-480)	Not included in article.	Not included in article.	Limitation = small sample size.
(Ernster et al., 1990)	Smokeless tobacco use and health effects among baseball players	Questionnaire plus clinical measures, 1,109 professional baseball players.	<ul style="list-style-type: none"> <li>• ≤1 = 42%</li> <li>• 2-3 = 37%</li> <li>• ≥4 = 22%</li> </ul>	Not included in article.	Not included in article.	<ul style="list-style-type: none"> <li>• 0.0-1.0 = 51.8%</li> <li>• &gt;1.0-2.0 = 25.3%</li> <li>• &gt;2.0 = 22.9%</li> </ul>	Not included in article.	Strengths/limitations = none noted.
(Severson et al., 1990)	The inside scoop on the stuff called snuff: an interview study of 94 adult male smokeless tobacco users	Survey, smokeless tobacco, 94 adult males, mean (SD) age of snuff consumers 32 (14.3).	Not included in article.	Mean = 10 (range, 1-40)	Just under 1 h, (range, 5 min to 4 h)	Not included in article.	<ul style="list-style-type: none"> <li>• Mean weight of a dip = 1.2 g (range, 0.1-7.3 g)</li> <li>• Number of days a can lasts Mean = 5 d</li> </ul>	Limitations = none noted.
(Daly & Pierson, 1990)	The use of smokeless tobacco among basic airmen	Survey questionnaire, 1,954 basic airmen.	Snuff mean cans/wk = 1.99 (range, 0.1-10.0)	Not included in article.	Not included in article.	Snuff mean min/d = 104.1 (range, 1.0-720)	Not included in article.	Limitations = unique population and limited number of measures.
(Colborn et al., 1989)	Correlates of adolescents' use of smokeless tobacco	Cross-sectional questionnaire, ST, 568 adolescents.	<ul style="list-style-type: none"> <li>• ≤1 can or pouch/wk = 38%</li> <li>• 2 cans or pouches/wk = 26%</li> <li>• 3-4 cans or pouches/wk = 26%</li> <li>• ≥1 cans or pouches daily = 10%</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Strengths/limitations = none noted.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Riley et al., 1989)	Typology and correlates of smokeless tobacco use	Questionnaires, ST, 3,725 high school students, Grades 9-12.	Not included in article.	<ul style="list-style-type: none"> <li>• ≤1 = 59.7%</li> <li>• 2-3 = 22.6%</li> <li>• ≥4 = 17.7%</li> </ul>	Not included in article.	<ul style="list-style-type: none"> <li>• &lt;1 h/d = 62.6%</li> <li>• 1-2 h/d = 19.5%</li> <li>• ≥3 h/d = 18.0%</li> </ul>	Not included in article.	Limitations = none noted
(Benowitz et al., 1989)	Daily use of smokeless tobacco: systemic effects	PK study, crossover design, oral snuff and chewing tobacco, 8 subjects, mean age = 49 years, age range = 27-61 years.	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Grams of smokeless tobacco consumed per day mean (SD) (range): <ul style="list-style-type: none"> <li>• Oral snuff = 15.6 (5.9) (range, 6.8-22.0)</li> <li>• Chewing tobacco = 72.9 (21.6) (range, 33.7-103.7)</li> </ul>	limitations = small sample size and limited topography measures.
(Schinke, Schilling, Gilchrist, Ashby, & Kitajima, 1989)	Native youth and smokeless tobacco: prevalence rates, gender differences, and descriptive characteristics	Questionnaires, ST, 119 Native American youth from Indian reservations in Washington State.	Cans, pouches, plugs used weekly: <ul style="list-style-type: none"> <li>• &lt;1 = 46.7%</li> <li>• 1 = 46.7%</li> <li>• 2-4 = 6.7%</li> <li>• &gt;4 = 0.0</li> </ul>	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = few topographical measures and unique population may not be generalizable.
(Hatsukami et al., 1988)	Topographical features of smokeless tobacco use	Survey, 56 male college-age ST consumers (mean age = 20.7 ± 1.9 years, age range = 18-30 years).	Mean (SD) = 2.8 (1.5)	Mean (SD) = 6.3 (2.2) (range, 2.5-12.5)	Mean (SD) = 39.9 (16.5) (range, 13.9-83.9)	Mean (SD) = 254.6 min (129.3) (range, 41-588 min)	Inter-dip interval mean (SD) = 102.6 min (42.1) (range, 41.1-240.5 min)	Strength = study specifically designed to measure topographical use patterns.
(Benowitz, Porchet, Sheiner, & Jacob III, 1988)	Nicotine absorption and cardiovascular effects with smokeless tobacco use: comparison with cigarettes and nicotine gum	PK-PD time-course study, oral snuff and chewing tobacco, 10 healthy volunteers (all men), aged 24-61 years.	Not included in article.	Not included in article.	Not included in article.	Not included in article.	“Typical dose” for oral snuff = 2.5 g	limitations = small sample size and few topography measures.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Ary et al., 1987)	Smokeless tobacco use among male adolescents: patterns, correlates, predictors, and the use of other drugs	Questionnaire data, ST, 3,023 adolescents, Grades 7-10.	Not included in article.	Mean (SD) = 5.3 (3.2)	10-20 = 58.2% >20 = 33.7% <10 = 8.2%	Not included in article.	Estimated dip size = 1.3 g	Strength = 9-month follow-up, limitation = data based on self-reports.
(Hatsukami, Gust, & Keenan, 1987)	Physiologic and subjective changes from smokeless tobacco withdrawal	Prospective examination of withdraw symptoms in , 16 ST consumers, age ≥18 years.	Mean (SD) = 2.06 (1.14)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitations = small sample size and few topographical measures.
(Marty, McDermott, & Williams, 1986)	Patterns of smokeless tobacco use in a population of high school students	Survey, ST, 901 high school students from Arkansas.	Not included in article.	<ul style="list-style-type: none"> <li>• 1 = 17.6%</li> <li>• 2-3 = 30.0%</li> <li>• 4-5 = 21.2%</li> <li>• 6-7 = 14.1%</li> <li>• 8-9 = 4.7%</li> <li>• ≥10 = 12.4%</li> </ul>	Not included in article.	Not included in article.	Frequency in days per week: <ul style="list-style-type: none"> <li>• ≤1 = 18.2%</li> <li>• 2-3 = 11.8%</li> <li>• 4-5 = 11.8%</li> <li>• 6-7 = 58.2%</li> </ul>	Limitation = few topographical measures.
(Marty, McDermott, Young, & Guyton, 1986)	Prevalence and psychosocial correlates of dipping and chewing behavior in a group of rural high school students	Survey, ST, 179 participants, mean age 15.9 years (range, 15-19 years).	Not included in article.	<ul style="list-style-type: none"> <li>• 1 = 6.7%</li> <li>• 2-3 = 40.0%</li> <li>• 4-5 = 23.3%</li> <li>• 6-7 = 16.7%</li> <li>• 8-9 = 0.0%</li> <li>• ≥10 = 13.3%</li> </ul>	<ul style="list-style-type: none"> <li>• ≤30 = 3.2%</li> <li>• 31-60 = 54.8%</li> <li>• 61-90 = 22.6%</li> <li>• 91-120 = 6.5%</li> <li>• &gt;120 = 12.9%</li> </ul>	Not included in article.	Frequency in days per week: <ul style="list-style-type: none"> <li>• ≤1 = 20.0%</li> <li>• 2-3 = 13.3%</li> <li>• 4-5 = 13.3%</li> <li>• 6-7 = 53.4%</li> </ul>	Limitations = none noted.
(Wisniewski & Bartolucci, 1989)	Comparative patterns of smokeless tobacco usage among major league baseball personnel	Survey, major league baseball personnel, (528 players, 80 managers/coaches, and 62 trainers), age range = 20-47 years.	Players: <ul style="list-style-type: none"> <li>• &lt;1/wk = 48.2%</li> <li>• 1-2/wk = 27.2%</li> <li>• 2-3/wk = 14.9%</li> <li>• &gt;3/wk = 9.7%</li> </ul>	Not included in article.	Not included in article.	Players: <ul style="list-style-type: none"> <li>• &lt;1 h = 48.2%</li> <li>• 1-2 h = 27.2%</li> <li>• 3-4-h = 14.9%</li> <li>• &gt;4 h = 9.7%</li> </ul>	Not included in article.	Limitation = few topographical measures.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
(Palladino, Adams, Brunnemann, Haley, & Hoffmann, 1986)	Snuff-dipping in college students: a clinical profile	Questionnaires plus biomarkers of exposure, 30 male students from an eastern military college.	Not included in article.	Not included in article.	Not included in article.	Minutes, mean (SD) = 200 (212)	Not included in article.	Limitation = limited topographical measures.
(Marty, McDermott, & Williams, 1986)	Smokeless tobacco use among rural high school students in Arkansas	Survey, ST, high school students (595 male, 606 female), mean age 16 years (range, 14-19).	Not included in article.	<ul style="list-style-type: none"> <li>Nearly every day = 84.0%</li> <li>2-3 dips/chews nearly every day = 13.4%</li> </ul>	<ul style="list-style-type: none"> <li>1 to 30 minutes = modal response</li> <li>In excess of 30 minutes = 30%</li> </ul>	Not included in article.	Not included in article.	Strengths/limitations = none noted.
(Greer & Poulson, 1983)	Oral tissue alterations associated with the use of smokeless tobacco by teen-agers. Part I. Clinical findings	Questionnaire plus clinical examinations, 117 ST consumers, high school students in Grades 9-12.	Not included in article.	"Use ranged from one to twenty "dips" per day..."	"...with an average time per dip of 30 minutes."	<ul style="list-style-type: none"> <li>Smokeless consumers with oral sequelae, average = 177 min</li> <li>Smokeless consumers with no oral sequelae, average = 53 min</li> </ul>	Not included in article.	Limitation = few topographical measures.
(Gritz, Baer-Weiss, Benowitz, Van, & Jarvik, 1981)	Plasma nicotine and cotinine concentrations in habitual smokeless tobacco users	Clinical study, ST, 12 male college students, mean age 19.8 ± 0.4 years (range = 18-22).	Not included in article.	Mean (SEM) = 8.8 (2.1)	Mean (SEM) = 24.2 (4.3)	Not included in article.	Inter-dip interval, mean (SEM) = 85 (2.4) min	Limitations = small sample size and limited topographical measures.
(Creath et al., 1988)	The prevalence of smokeless tobacco use among adolescent male athletes	Survey, dip, chewing tobacco, 995 adolescent male football players.	<ul style="list-style-type: none"> <li>&lt;1 tin/wk = 78.2%</li> <li>1 tin/wk = 11.1%</li> <li>1-2 tins/wk = 6.6%</li> <li>≥3 tins/wk = 4.1%</li> </ul>	Not included in article.	Not included in article.	<ul style="list-style-type: none"> <li>&lt;1 h/d = 79.2%</li> <li>1-2 h/d = 14.5%</li> <li>3-4 h/d = 1.7%</li> <li>&gt;4 h/d = 3.5%</li> </ul>	Not included in article.	Strength = large sample size, limitation = unique population may not be generalizable.

Reference	Title	Study Methods, ST Products Evaluated, Study Participants	Cans <sup>1</sup> per Week	Dips per Day	Dip Duration per Dip (minute)	Dip Duration per Day	Other Measures	Comments
( <a href="#">Martin, Brown, Eifler, &amp; Houston, 1999</a> )	Oral leukoplakia status six weeks after cessation of smokeless tobacco use	Case control study, 3,051 male U.S. Air Force basic training personnel, mean age 19.5 years.	Average cans (SD) per day = 0.52 (0.42)	Not included in article.	Not included in article.	Not included in article.	Not included in article.	Limitation = few topographical measures.

**Table 7.5.8-1-3: Literature Related to Misuse of Tobacco Products**

Reference	Title	Study Characteristics	Findings
(Appleton, 2011)	Frequency and outcomes of accidental ingestion of tobacco products in young children	Analysis of 27 years of data from poison control centers for occurrence and outcomes associated with accidental ingestions of tobacco products among young children. Strength = large data set; limitations = events are self-reports, and a significant number of exposure events are not assigned outcome categories.	“Based on this assessment of surveillance and case study reports, the frequency and severity of outcomes associated with accidental ingestion of tobacco products by young children appear to be relatively low.”
(Garcia-Estrada & Fishman, 1977)	An unusual case of nicotine poisoning	Case report of a 54-year-old man whose family claimed that he had given himself an enema. Strengths/limitations = case report.	“We have recently treated an adult for acute nicotine poisoning from a tobacco enema. This unusual case allowed us to observe some of the complex pharmacologic responses of the body to nicotine.”
(O’Berst & McIntyre, 1953)	Acute nicotine poisoning; case report	Case report of a 2.5-year-old male child whose grandmother attempted to treat intestinal worms with an enema of tobacco extract. Limitation = case report.	“A case of acute nicotine poisoning due to a tobacco infusion given per enema is described.” The child was treated and recovered in 18 hours.
(Schneider et al., 2010)	Internet suicide guidelines: report of a life-threatening poisoning using tobacco extract	Case report of a 67-year-old man who tried to commit suicide by following guidelines found on an Internet site. Limitation = case report.	“He soaked 300 grams of tobacco for 3 days in water, evaporated most of the extract, and drank the rest of it.” The patient was treated by an emergency medical care team, placed in an intensive care unit, and was discharged 4 days later “with no visible sequelae.”
(Smolinske et al., 1988)	Cigarette and nicotine chewing gum toxicity in children	Prospective review of 51 cases of tobacco ingestion in children. Limitation = limited number of cases.	“This study would suggest that children who ingest more than one cigarette or 3 cigarette butts are more likely to develop significant toxicity, and should be observed in a health care facility.”
(Willis, 1937)	Acute nicotine poisoning	Case report of a 5-year-old male child whose mother had noticed pinworms. The tobacco juice enema was a misdirected effort at medication. Strengths/limitations = case report.	“A history obtained was that one hour previous to admission the child was given an enema consisting of 60 c.c. of strong tobacco juice in 1,000 c.c. of water.”  “The child was kept alive for some time by alternating periods of artificial respiration but died in one of the periods when his condition seemed favorable.”

## 7.5.8-1.6.Literature Cited

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