



# Topography of Dissolvable Tobacco Products

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The information in these materials is not a formal dissemination of information by FDA and does not represent agency position or policy. The information is being provided to TPSAC to aid the committee in its evaluation of the issues and questions referred to the committee.

# Overview

- General product information
- Background
- Topography of smokeless tobacco products
- Topography of dissolvable tobacco products (DTPs)

# Some of the Currently Available DTPs in the U.S.



# Recently Available DTPs in the U.S.



# Nicotine Loads by Product

- Ariva: 1.5 mg nicotine
- Stonewall: 4 mg nicotine
- Camel:
  - Strip - 0.6 mg
  - Orb -1 mg
  - Stick - 3 mg
- NicoSpan 1 mg
- Viceroy Flex - not publicly available
- Skoal Stick - not publicly available
- Marlboro Stick - not publicly available

# Background

- Topography assesses human tobacco consumption behavior
- With smokeless tobacco (ST), topography measures include: self-reported measures of tobacco use such as ST tins used per week, total daps per day, total daily dip duration, and total daily dipping time (time from first dip in the morning until last dip of the day).
- Dissolvable tobacco product topography measures could include quantity, frequency, and duration of use.

## Background (Cont.)

- There currently exists no standardized method for measuring the topography of oral tobacco product use
- Currently, there is very limited information available on topography of dissolvable tobacco products
- What can we learn from experiences of other tobacco products to help us understand what topography might be expected from dissolvable products?

# Topography of Smokeless Tobacco

- Male smokeless tobacco (ST) users aged 21-65 recruited for a study comparing nicotine replacement products and new tobacco products.
- Participants had used at least one tin of ST per week for a minimum of 1 year.
- During 2 weeks of baseline *ad libitum* ST use, 54 participants (mean age  $32.1 \pm 7.5$  years) recorded the time each dip was placed in and removed from mouth.

## 2005 Study by Lemmonds et al.

- Outcome measures: nicotine, cotinine, glucuronides (total nicotine and total cotinine) NNK, total NNAL
- The results suggest that frequency and duration measures of ST use ( $p < .01$  to  $p < .001$ ), particularly total dip duration, are significantly correlated with total cotinine, total nicotine, and total NNAL.

# Example of ST Topography Measures

**Table 1.** Tobacco use and carcinogen exposure.

Variable	N	Median	Mean ± standard deviation
Quit attempts	52	4.0	7.8 ± 14.1
Tobacco brand			
Copenhagen, fine cut	15		
Copenhagen, long cut	4		
Kodiak, fine cut	5		
Kodiak, long cut	20		
Skoal, long cut	7		
Other	3		
Years of smokeless tobacco use	54	12.0	12.5 ± 5.8
Dips/day	54	6.1	6.8 ± 3.0
Tins/week	53	2.8	3.4 ± 2.8
Average total daily dip duration, minutes <sup>a</sup>	53	388.0	423.0 ± 224.4
Average daily dip duration of an individual dip, minutes <sup>b</sup>	53	61.6	71.2 ± 44.3
Total daily dipping time, minutes <sup>c</sup>	54	860.0	820.6 ± 120.4
Total nicotine, nmol/mg creatinine	54	9.9	10.5 ± 5.6
Total cotinine, nmol/mg creatinine	54	20.1	23.5 ± 14.3
Total nicotine+total cotinine, nmol/mg creatinine	54	30.6	34.0 ± 18.3
Total NNAL, pmol/mg creatinine	54	2.9	3.3 ± 2.1

Notes. NNAL, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronides.

<sup>a</sup>Total number of minutes per day that dip was in the mouth.

<sup>b</sup>Average daily number of minutes that an individual dip was in the mouth.

<sup>c</sup>Time from first dip in the morning until last dip of the day.

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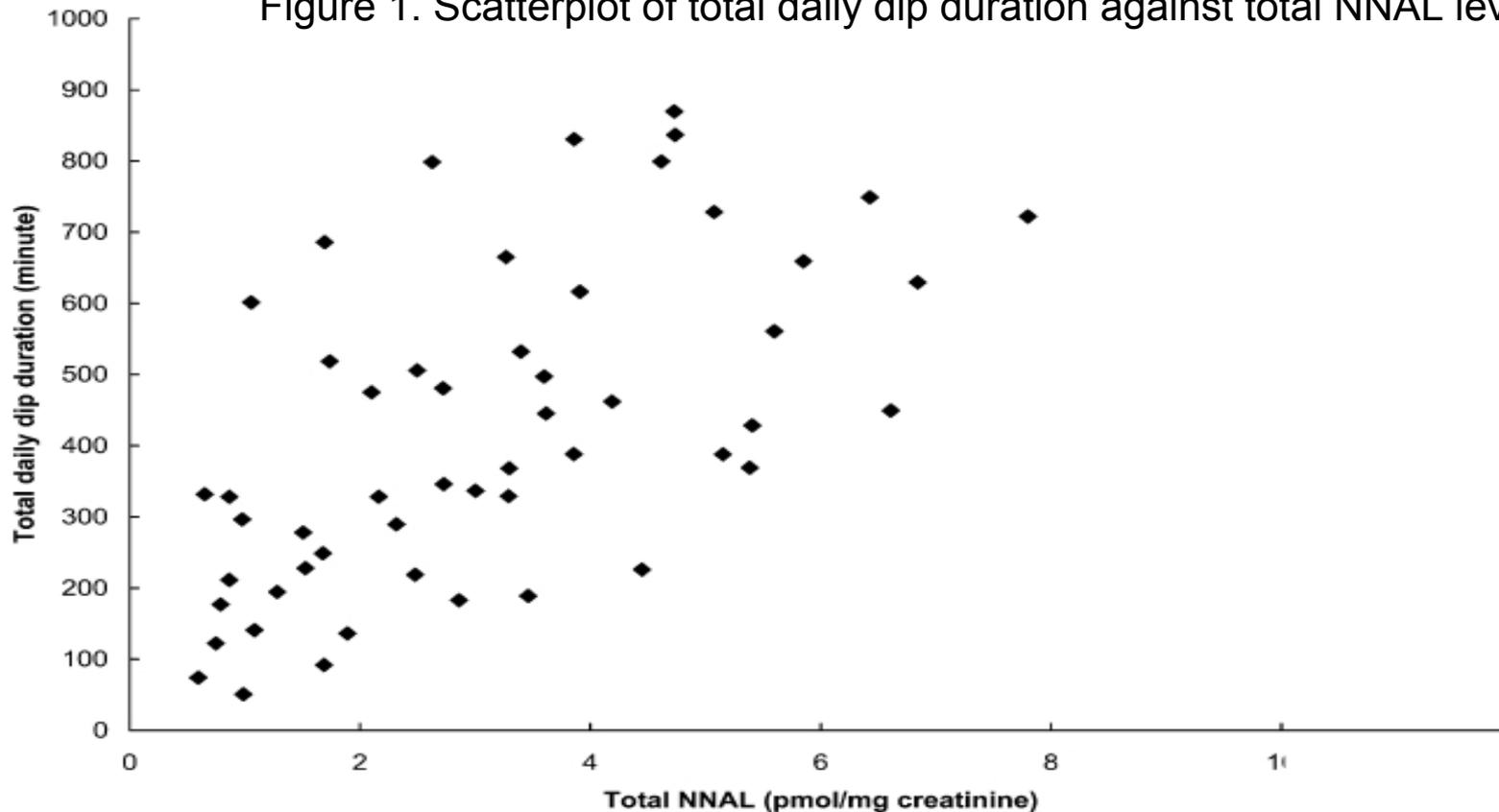
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<sup>b</sup>Average daily number of minutes that an individual dip was in the mouth.

<sup>c</sup>Time from first dip in the morning until last dip of the day.

# Total NNAL levels Increase as Total Daily Dip Duration Increases

Figure 1. Scatterplot of total daily dip duration against total NNAL level.



Lemmonds et al. Smokeless tobacco topography and toxin exposure. *Nicotine and Tobacco Research*. 2005; 7(3): 469-474.

# Topography of DTPs

- TPSAC requested information on the variability of how DTP's are used\*
- 3 studies referenced:
  - Gray et al. (2008); Blank et al. (2010); Carpenter and Gray (2010)
  - Data provided for topography measures
- Studies were provided in the background materials and are publicly available
- Conclusions drawn are the author's and not FDA

(\*<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM270283.pdf>)

# 2008 Study by Gray et al.

- Type of study: clinical laboratory study
- Use of DTP:
  - Stonewall
  - 5 days *ad libitum*
  - solely DTP use
  - per package instructions, participants were asked to place the product in their mouth and allow it to dissolve (~15-min duration) without chewing or swallowing

# 2008 Study by Gray et al. (cont)

- Participant description: 19 participants (0 women), between 18 and 50 years ( $M = 24.0$ ,  $SD = 12.2$ ) who had used  $\leq 5$  smoked tobacco products during the past 6 months and reported current use of ST on a daily basis ( $M = 5.2$ ,  $SD = 3.4$ ) for the last 12 months ( $M = 8.1$ ,  $SD = 6.8$ )
- Objectives: To adapt models used to examine cigarette-like PREPs for smokers for use in the evaluation of toxicant exposure and abstinence symptom suppression for ST users

## 2008 Study by Gray et al. (cont)

- Author conclusions:
  - Amount of DTP used expressed as a percentage of product provided was significantly higher for Stonewall ( $M = 45.3\%$ ,  $SEM = 5.1$ ,  $p < .01$ ) vs. General snus ( $M = 31.7\%$ ,  $SEM = 3.8$ ) and own brand of ST ( $M = 49.2\%$ ,  $SEM = 5.4$ )
  - Stonewall had lower CO, cotinine and NNAL levels vs. own brand ST

# 2010 Study by Blank et al.

- Type of study: clinical laboratory study
- Use of DTP:
  - Ariva
  - 5 days *ad libitum*
  - solely DTP use
  - per package instructions, participants were asked to place the product in their mouth and allow it to dissolve (~15-min duration) without chewing or swallowing

## 2010 Study by Blank et al. (cont)

- Participant description: 21 participants (6 women), between 18 and 55 years ( $M = 33.3$ ,  $SD = 13.0$ ) who had used  $\geq 15$  cigarettes ( $M = 20.4$ ,  $SD = 5.3$ ) at least one year ( $M = 8.0$ ,  $SD = 7.1$ )
- Objectives: Measure toxicant exposure, abstinence symptom suppression in smokers

# 2010 Study by Blank et al. (cont)

- Author conclusions:
  - During 5 day conditions the mean number of Ariva consumed collapsed across the day factor was 12.3 ( $SEM = 0.88$ ) vs. 21.9 ( $SEM = 0.77$ ) cigarettes, 11.7 ( $SEM = 0.79$ ) snus
  - Average scores for “Are the tobacco products you are using this week pleasant?” were significantly lower for Ariva vs. cigarettes, higher for Ariva vs. snus
  - Ariva had lower CO, cotinine but not NNAL levels vs. cigarettes, similar CO, cotinine and NNAL vs. snus

# 2010 Study by Carpenter and Gray

- Type of study: clinical trial
- Use of DTP:
  - Stonewall
  - 14 days *ad libitum*
  - Used concurrently with cigarettes
  - per package instructions, participants were asked to place the product in their mouth and allow it to dissolve (~15-min duration) without chewing or swallowing

Carpenter, M.J. & Gray, K.M. A pilot randomized study of smokeless tobacco use among smokers not interested in quitting: Changes in smoking behavior and readiness to quit. *Nicotine and Tobacco Research*. 2010; 12(2): 136-143.

# 2010 Study by Carpenter and Gray

- Participant description: 19 participants (7 women), between 18 and 55 years ( $M = 42.2$ ,  $SD = 14.1$ ) who had used  $\geq 10$  cigarettes ( $M = 24.4$ ,  $SD = 10.2$  weekday;  $M = 26.0$ ,  $SD = 11.9$  weekend) at least one year (age started smoking regularly  $M = 16.0$ ,  $SD = 3.0$ )
- Objectives: Measure influence of short term ST use on smoking behavior and cessation in smokers unmotivated to quit
  - participants were told of the study purpose: to measure changes in smoking behavior while using the new tobacco product.

# 2010 Study by Carpenter and Gray

- Author conclusions:
  - DTP use was an average of 7.7 ( $SE = 1.7$ ) pieces/day Week 1 and 7.5 ( $SE = 1.2$ ) pieces/day Week 2
  - 50% of participants used DTP “more than a few times” or “frequently” to cut down on their cigarettes smoked; 39% used DTP to cope or avoid smoking restrictions. DTP use was more predominant to avoid smoking restrictions at work (44% vs. use at home (33%).

# Study limitations

- Studies were not designed specifically to examine topography.
- Most studies examined users of combustible tobacco products, not users of DTPs.
- Studies did not assess compliance of DTP use/uncontrolled use of other products.
- Studies were of a short 1-2 week duration; not enough time to establish consistent DTP use behavior.

# Summary

- There currently exists no standardized method for measuring the topography of oral tobacco product use
- More clinical research is needed as well as standardized clinical evaluation processes to evaluate the topography of DTPs