

# Comparisons Between Adult Menthol and Non-Menthol Smokers – Total Exposure Study

Mohamadi Sarkar, M.Pharm., Ph.D  
Altria Client Services



# Outline

- Background
  - Information provided
  - Total Exposure Study (TES) overview and key conclusions
  - Questions raised by the TPSAC members
- Additional analysis of the TES Data from adult smokers of  $\leq 10$  cigarettes per day
  - Biomarkers of Exposure in adult smokers
  - Fagerstrom Test for Nicotine Dependence (FTND) scores
  - Time to First Cigarette (TTFC)



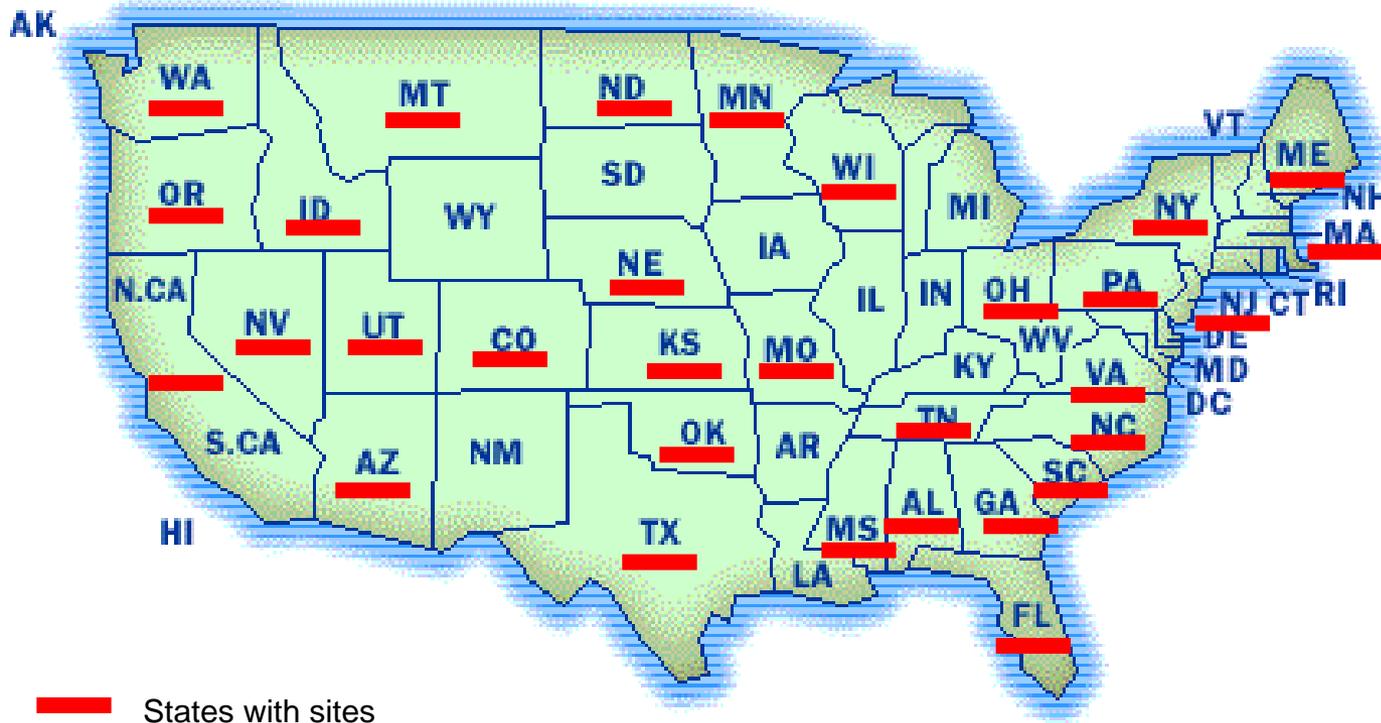
# Information Provided

- Written submissions
  - March 22, 2010
  - June 30, 2010
- Presentations on five topical areas, including Biomarkers – July 15, 2010
- Provided menthol-related documents – August 25, 2010
- Total Exposure Study (TES) Dataset – August 25, 2010



# PM USA Total Exposure Study -TES

- The TES was a stratified, multi-center, cross-sectional study that had 3585 evaluable adult smokers and 1077 evaluable adult non-smokers from 31 states (39 investigative sites) across the U.S.



# Objectives of the TES

- Primary objectives:
  - To estimate the exposure of U.S. adult cigarette smokers to selected cigarette smoke constituents
  - To investigate the relationship between cigarette smoke exposure of U.S. adult smokers and tar delivery <sup>a</sup>
- Secondary objectives:
  - To compare selected biomarkers of U.S. adult smokers to adult non-smokers
  - To evaluate smoking behaviour as it relates to cigarette smoke exposure
  - To investigate the relationship between selected biomarkers of potential harm and cigarette smoke exposure

<sup>a</sup> Measured by the Cambridge filter method



# Summary of Key Results – Presented to TPSAC on 7/15/2010

- Based on the selected biomarkers of exposure investigated, cigarette smoke exposure in adult menthol smokers was not statistically significantly different compared to that observed in non-menthol smokers
- Menthol does not appear to inhibit the metabolism of nicotine or NNK
- Menthol had no statistically significant effect on the biomarkers of potential harm investigated
- Menthol cigarette smokers did not have higher Fagerström Test for Nicotine Dependence (FTND) scores compared to non-menthol cigarette smokers



# Some Questions Raised by TPSAC Members

Quoted from the TPSAC Meeting Transcripts

- "...could you do an analysis of just 10 or fewer cigarettes per day and looking at biomarkers as a function of menthol?" Dr. Benowitz (7/15/2010)
- "I'd like to see what the FTND scores are by menthol cigarettes among people that are smoking few cigarettes.. Similar to what Neal was asking...." Dr. Hatsukami (7/15/2010)
- ".....there's only one human study, which was one that I published. But there also are studies in liver microsomes; one published study and one unpublished study showing that nicotine inhibits menthol metabolism and microsomes." Dr. Benowitz (1/10/2011)
- "I think another issue which is important is when you look at dependence with the FTND it's looking at cigarettes per day.." Dr. Samet (1/10/2011)
- "But in a recent study it basically said there may be a sweet spot, in other words people who smoke six to 10 cigarettes per day seem to have to have that cigarette earlier than others." Dr. Clanton (1/10/2011)
- "Did you try to do any analysis of the source data like the total exposure study?" Dr. Benowitz (1/10/2011)



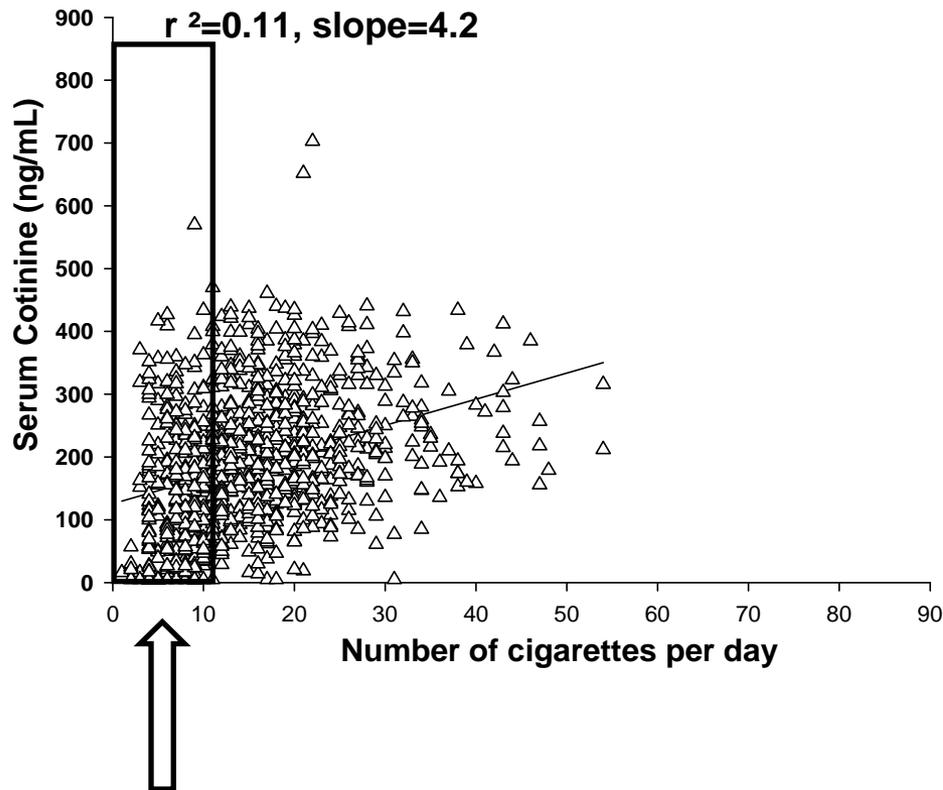
# Objective of the Additional Analysis of the TES Dataset

- To determine whether there are any differences in biomarkers of exposure and dependence measures in the sub-group of adult menthol and non-menthol smokers of  $\leq 10$  cigarettes per day (CPD)



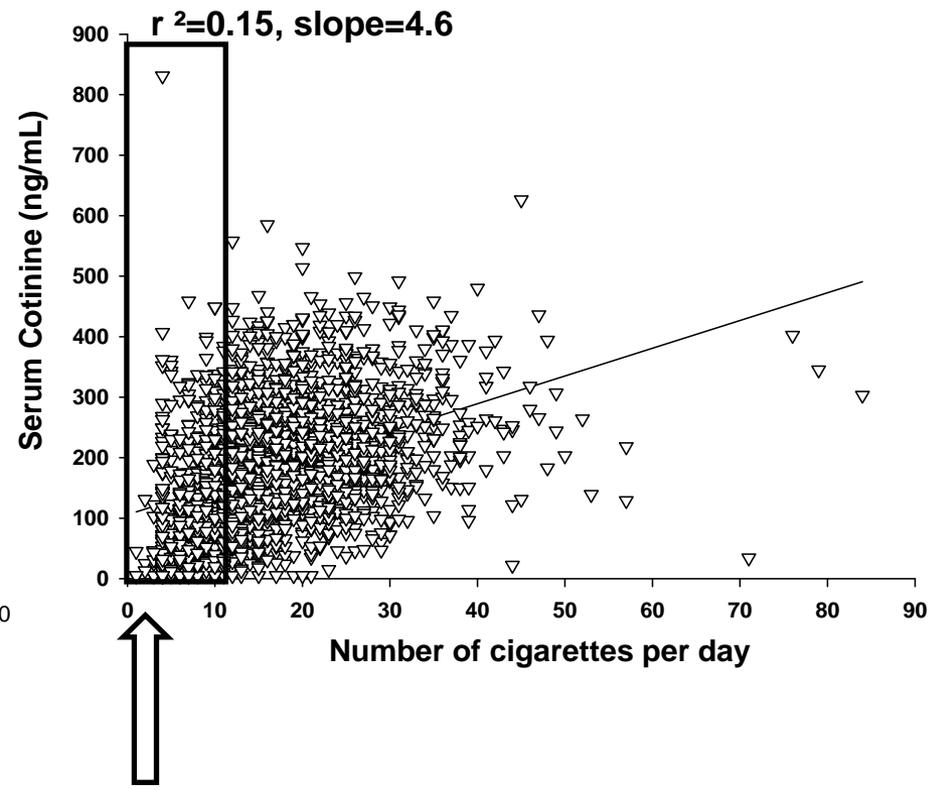
# Relationship Between Serum Cotinine and CPD\*

## Adult Menthol Smokers (n=979)



Subset smoking  $\leq 10$  CPD

## Adult Non-Menthol Smokers (n=2189)



Subset smoking  $\leq 10$  CPD

\*CPD=Cigarettes Per Day



# Demographic Characteristics Adult Smokers of $\leq 10$ Cigarettes Per Day

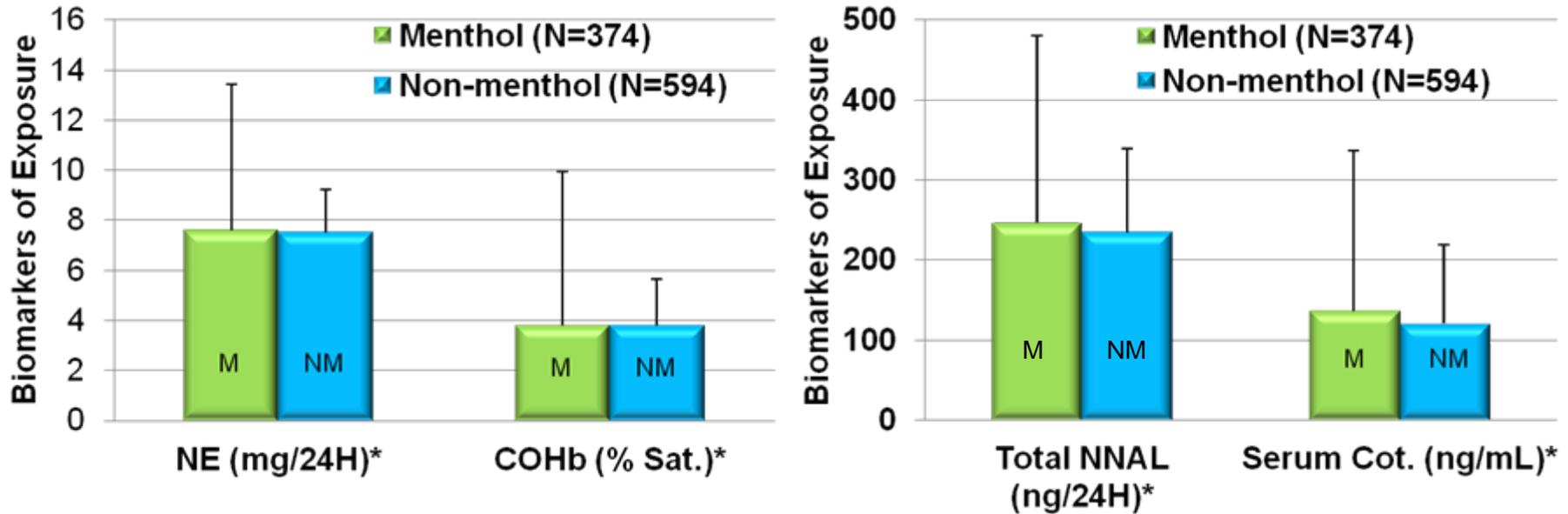
	<b>Menthol (N=374)</b>	<b>Non-menthol (N=594)</b>
<b>Age (years, mean (SD))</b>	38.6 (11.8)	38.9 (13.7)
<b>Gender, No. (%)</b>		
Female	237 (63.4%)	337 (56.7%)
Male	137 (36.6%)	257 (43.3%)
<b>Race, No. (%)</b>		
African-American	246 (65.8%)	87 (14.7%)
White	128 (34.2%)	507 (85.3%)
<b>BMI (kg/m<sup>2</sup>), Mean (SD)</b>	29.3 (7.5)	26.9 (6.7)
<b>CPD<sup>a</sup>, Mean (SD)</b>	7.1 (2.2)	7.2 (2.2)
<b>Tar Yield (mg), Mean (SD)</b>	11.4 (6.5)	7.6 (5.0)
<b>Years Smoking, Mean (SD)</b>	16.1 (11.8)	17.7 (13.5)

<sup>a</sup> Number of cigarettes smoked per day, based on number of butts returned



# Biomarkers of Exposure in Adult Smokers of $\leq 10$ CPD

Descriptive Statistics



Overall, based on the statistical models, biomarkers of exposure were not significantly higher in adult menthol smokers compared to non-menthol smokers

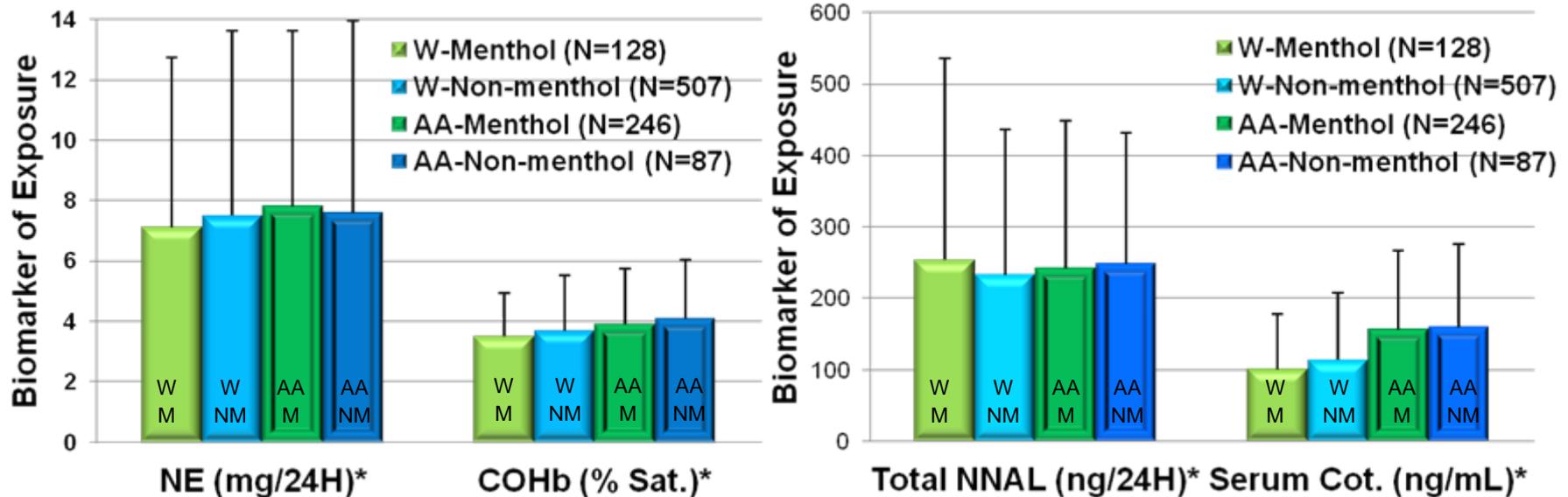
Data Shown as unadjusted Mean+SD; \*Number of evaluable observations varied for each biomarker

NE=Nicotine Equivalent (Nicotine and five of its metabolites); COHb=Carboxyhemoglobin; Total NNAL=NNK metabolites (Free NNAL and Glucuronide conjugates)



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# Fagerström Test for Nicotine Dependence (FTND) Adult Smokers of $\leq 10$ CPD

<b>Categorization of FTND Scores</b>	<b>Menthol Status</b>	<b>Adjusted<sup>a</sup> Odds Ratio</b>	<b>95% CI</b>
<b>Five Categories</b> (Very Low: 0-2 points, Low: 3-4 points, Medium: 5 points, High: 6-7 points, Very High: 8-10 points)	<b>Menthol</b>	<b>1.07</b>	<b>0.79 – 1.46</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>
<b>Three Categories</b> (Low (0-3), Medium (4-5) and High (6-10) scores)	<b>Menthol</b>	<b>0.95</b>	<b>0.68 – 1.32</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>
<b>Two Categories</b> (Low/Medium (0-5) and High (6-10) scores)	<b>Menthol</b>	<b>1.34</b>	<b>0.73 – 2.45</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>

<sup>a</sup> Adjusted for age, race, gender, education and tar yield category.

Overall, based on the statistical model no significant effect of menthol was observed on FTND, regardless of how the scores were categorized.



# Time to First Cigarette (TTFC) Adult Smokers of $\leq 10$ CPD

<b>Categorization of TTFC</b>	<b>Menthol Status</b>	<b>Adjusted<sup>a</sup> Odds Ratio</b>	<b>95% CI</b>
Four Categories ( $\leq 5$ mins, 6-30 mins, 30-60 mins and $\geq 60$ mins.)	<b>Menthol</b>	<b>0.89</b>	<b>0.66 – 1.19</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>
Two Categories ( $\leq 30$ mins and $> 30$ mins)	<b>Menthol</b>	<b>1.01</b>	<b>0.72 – 1.42</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>
Two Categories ( $\leq 5$ mins and $> 5$ mins)	<b>Menthol</b>	<b>0.89</b>	<b>0.55 – 1.45</b>
	<b>Non-Menthol</b>	<b>1.00</b>	<b>Reference</b>

<sup>a</sup> Adjusted for age, race, gender, education and tar yield category.

Overall, the analysis of TTFC showed that the odds of smoking within  $\leq 5$  minutes of waking were not statistically significantly higher in adult menthol smokers compared to nonmenthol smokers



# Conclusions

- Exposure and dependence measures were not significantly higher in menthol as compared to non-menthol adult smokers of  $\leq 10$  CPD.
- These results are consistent with the previous findings from the TES, observed among all adult smokers.
- The results of this analysis adds to the substantial body of evidence which indicates no effect of menthol on exposure or dependence measures.

