TITLE: A cross-sectional study to evaluate product knowledge and product use after initiation of VLN™ cigarettes
PRODUCT: VLN™ Kings and VLN™ Menthol Kings
STUDY No.: <to be determined>

Rationale and background	VLN™ cigarettes are a new smokable very low nicotine tobacco product This study is being done to address FDA requirements for post-approval evidence of consumer knowledge and usage of VLN™ cigarettes. The proposed study utilizes a cross-sectional study design of 1000 individuals up to six months after their initiation of VLN™ cigarettes.

Research question and objectives	The specific objectives are:
	
	• Primary objectives
	
	    o assess knowledge of VLN™ cigarettes product characteristics
	
	    o assess usage patterns of VLN™ cigarettes
	
	    o assess demographic (age, gender, ethnicity, three digit zip code) characteristics of VLN™ cigarette users
	
	• Secondary objectives:
	
	    o assess use of other tobacco products used at time of initiation of VLN™ cigarettes
	
	    o describe how user learned about VLN™ cigarettes
	
	    o describe personal factors motivating initiation to VLN™ cigarettes

Study design	This is a cross-sectional study to evaluate knowledge, use, and attitudes of new users of VLN™ cigarettes. The study will be conducted among U.S. individuals who have initiated VLN™ cigarettes within the past 6 months. The target number of users completing the study is 1000. Users will be recruited from the general population in the U.S. Each user agreeing to be in the study will be sent a link to an online study portal. The study portal will include the process for the user to: 1) consent to participate in the study; 2) consent for the contract research organization running the study to contact the user for additional personal contact information and the ability to invite for participation into other studies 3) complete the web-based data collection forms for the subject to fill out on all study information. 4) information about who to contact with any issues in use of the study portal or completion of the data collection forms. Prior to launching the study, the draft data collection forms will undergo cognitive pre-testing in a small separate group of VLN™ cigarette users (n=10). The goals of cognitive pre-testing are to identify any questions that require clarification or

	revision based on areas of confusion or miscomprehension revealed by subjects in the cognitive pre-test interviews.
	Users will be paid for completion of the study data collection forms for the entire study based on guidelines in the USA for appropriate compensation for their time to complete all study related activities. This is estimated to be USD $25.00.
Population	Inclusion criteria: • Initiation of VLN™ cigarettes after FDA approval for general sale in the USA. • Provide permission to share their responses in aggregate with FDA or tobacco regulatory within and outside of the USA, if requested Exclusion criteria: • Participated in the cognitive pre-testing of the survey questionnaire

Variables	The survey questionnaire includes the following:
	
	• Questions regarding user demographic characteristics (age, gender, ethnicity, USA postal zipcode of residence – first three digits only)
	
	• Questions to assess usage of tobacco
	
	    o Estimated usage of other nicotine/tobacco products in past three months:
	
	        ▪ cigarettes (usual brand of cigarettes including roll your own, average number of cigarettes per day),
	
	        ▪ cigars (number per day), pipe usage (number of times per day),
	
	        ▪ other non-smoked tobacco products (average amount of oral and nasal tobacco products),
	
	        ▪ and nicotine containing products (type of product and average amount used).
	
	• Questions about knowledge and usage of VLN™ cigarettes
	
	    o Estimated number of VLN™ cigarettes smoked per day on each of the preceding 7 days. This question will require the user to estimate the number of VLN™ cigarettes smoked on each day of the week.
	
	    o Usage of other tobacco and nicotine containing products in the preceeding 7 days. (type and number of cigarettes, number of cigars, times pipe smoked, type and number of times used nicotine containing products)
	
	    o Describe how the user became aware of VLN™ cigarettes. Details on types of communication that alerted user to existence of VLN™ cigarettes (website, point of sale information, friend, health care provider)
	
	    o Describe personal factors motivating the decision to start smoking VLN™ cigarettes (health concerns about smoking, desire to reduce smoking, desire to quit smoking, interest in trying new product)

Data sources	All data will be collected by on-line data capture from study participants in the U.S.
Study size	A sample of 1000 completed subjects is targeted for this study. This sample size was based on both feasibility and statistical considerations.
Data analysis	The primary analysis population will include all subjects who have completed the survey.
	Generally, categorical outcomes will be described by the absolute and relative (%) frequency of each outcome and number of missing data. Missing data will be taken into account in the percentage calculation. If appropriate, 95% Confidence Iintervals for proportions will be calculated for the key categorical outcomes. Quantitative variables generally will be described by their mean, standard deviation, median, and number of missing data. Results for some quantitative variables may also include ranges (minimums and maximums).
	<u>Sample Size</u>
	A sample of 1000 completed surveys is targeted for this study. Although all efforts will be made to reach the target, the actual sample size will depend on subjects' willingness to participate in the study.
	The target sample size was estimated based on the desire to have sufficient precision of estimates for the various outcomes of interest for this study, including ensuring adequate precision for anticipated subgroup analyses. Table 1 provides the precision and 2-sided 95% confidence interval (CI) around various rates that may be observed for several outcomes of interests for this study. For example, a sample size of 1000 subjects allows estimation of a 75% rate of use of VLN™ with a precision of 2.7% (Table 1).
Milestones	Start of data collection:
	End of data collection :
	Final report of study results :

Table 1: Precision and 95% Confidence Intervals for Various Sample Size and Outcome Rates.

Sample Size	Various Rates of Outcomes							
	25%		50%		75%		90%	
	Precision (%)	95% CI	Precision (%)	95% CI	Precision (%)	95% CI	Precision (%)	95% CI
250	5.4%	19.6-30.4	6.2%	43.8-56.2	5.4%	69.6-80.4	3.7%	86.3-93.7
500	3.8%	21.2-28.8	4.4%	45.6-54.4	3.8%	71.2-78.8	2.7%	87.4-92.6
750	3.1%	21.9-28.1	3.6%	46.4-53.6	3.1%	71.9-78.1	2.2%	87.9-92.1
1000	2.7%	22.3-27.7	3.1%	46.9-53.1	2.7%	72.3-77.7	1.9%	88.1-91.9

Note: Calculated using PASS 13 software,* confidence intervals for 1 proportion, simple asymptotic formula. Hintze, J. (2014). PASS 13. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.